Attorney Docket No. VPI/02-115 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.:	10/696,862
Confirmation No.:	8080
Filing Date:	October 30, 2003
Examiner:	Venkataraman Balasubramanian
Group Art Unit:	1624
Technology Center:	1600
Applicants:	Jingrong Cao et al.
For:	COMPOSITIONS USEFUL AS INHIBITORS OF ROCK AND OTHER PROTEIN KINASES

September 11, 2009
Cambridge, Massachusetts

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDED APPEAL BRIEF UNDER 37 C.F.R. §41.37(d)

Sir:

Applicants filed a Notice of Appeal and a Pre-Appeal Brief Request for Review on July 14, 2008 in the above-identified application. On July 10, 2009, a Notice of Panel Decision from Pre-Appeal Brief Review was mailed, stating that the rejection is maintained and that the application remains under appeal because there is at least one actual issue for appeal. Consequently, applicants timely filed an Appeal Brief on August 3, 2009 to accompany the Notice of Appeal. A Notification of Non-Compliant Appeal Brief was mailed on September 3, 2009, requesting that the appealed claims be identified. The Notification set a one-month deadline of October 3, 2009 for the filing of an amended brief. Consequently, this brief is timely submitted.

A Table of Contents is found on page 2 of this Amended Brief.

Applicants: Jingrong Cao et al.
Application No.: 10/696,862
Technology Center: 1600

TABLE OF CONTENTS

REAL PARTY OF INTEREST

The real party of interest in this appeal is:

Vertex Pharmaceuticals, Inc.

130 Waverly Street

Cambridge, MA 02139

RELATED APPEALS AND INTERFERENCES

There are no prior or pending appeals, judicial proceedings or interferences known to the appellant which may be related to, directly affect or be directly affected by, or have a bearing on the Board's decision in the pending appeal.

STATUS OF CLAIMS

Claim 1 – rejected

Claims 2-3 – canceled

Claims 4-5 – rejected

Claims 6-7 – canceled

Claims 8-12 – rejected

Claim 13 – canceled

Claims 14-20 – rejected

Claims 21-22 – canceled

Claims 23-29 – rejected

Claim 30 – canceled

Claim 31 – rejected

Claim 32 – canceled

Claims 33-46 – rejected

Claims 47-53 – canceled

Claims 54-57 – rejected

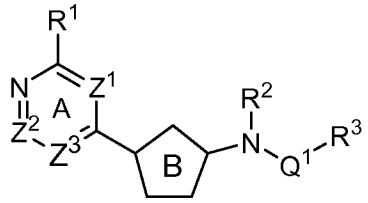
Applicants appeal the rejection of claims 1, 4-5, 8-12, 14-20, 23-29, 31, 33-46, and 54-57.

STATUS OF AMENDMENTS

No amendment has been filed in the present application after the Final Office Action.

SUMMARY OF CLAIMED SUBJECT MATTER

Claim 1 recites compounds having the following formula I:



I,

wherein R^1, R^2, R^3, Z^1, Z^2, Z^3, Q^1, and ring B are fully described in the specification in paragraph [0031] on pages 12-13.

Each of the remaining pending claims is dependent on claim 1.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The matter to be reviewed under appeal is whether claims 1, 4-5, 8-12, 14-20, 23-29, 31, 33-46, and 54-57 are unpatentable under 35 U.S.C. S 103(a) over Inaba et al., Japanese Patent Application No. 2002053566. A machine-translated version of Inaba is provided in the Evidence Appendix.

ARGUMENT

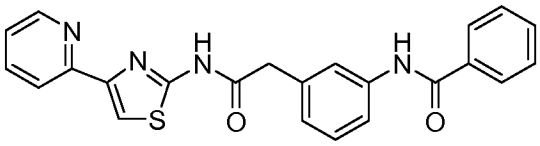
The obviousness rejection

In the November 1, 2007 Office Action (hereafter, "the November Office Action") and in the April 16, 2008 Final Office Action (hereafter, "the Final Office Action"), the Examiner rejected claims 1, 4, 5, 8-12, 14-20, 23-29, 31, 33-46, and 54-57 of the instant application under 35 U.S.C. § 103(a) for allegedly being obvious over Inaba et al., Japanese Patent Application No. 2002053566 (hereafter, "Inaba," provided as a machine-translated copy in the Evidence Appendix). In particular, the Examiner asserted that the compounds of Inaba are kinase inhibitors useful for the treatment of Alzheimer's disease and allergy, and that some of the compounds of Inaba are positional isomers of the compounds of the present invention, therefore making the compounds of the present invention not patentably distinct. The Examiner concluded with the reasoning from *KSR International Co. v. Teleflex Inc.*, 550 U.S. 1727, 1741 (S. Ct. 2007, hereafter "KSR") that "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense."

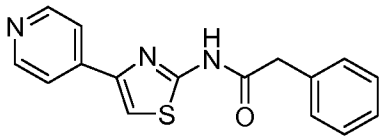
As held in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (S. Ct. 1966, hereafter "Graham"), and upheld in KSR, an obviousness determination turns on underlying factual inquiries involving the following factors: (1) the scope and content of the prior art, (2) differences between the claims and the prior art, (3) the level of ordinary skill in the pertinent art, and (4) secondary considerations such as commercial success and satisfaction of a long-felt need. As will be discussed below, the Examiner failed to make a *prima facie* case of obviousness because the factual inquiries used in the evaluation of the Graham factors outlined above were deficient.

Scope and content of the prior art relating to compound structure was not properly established

In the Final Office Action, the Examiner asserted that the compounds of Inaba are closely related positional isomers of the compounds of the present invention and therefore, it would have been obvious to one skilled in the art at the time the invention was made to expect the compounds of the present invention to possess the utility taught by the compounds of Inaba because the claimed compounds were not patentably distinct. The Examiner particularly pointed out Inaba compounds 51 and 80 (structures shown below) and stated that there was no proviso in claim 54 of the instant application to exclude these compounds. In response, applicants traversed for the following reasons: (i) pending claim 54 is dependent upon claim 1, which excludes compound 80; (ii) there is no reason to exclude compound 51 since it is outside the scope of claim 1; (iii) the Inaba compounds that were cited by the Examiner represent only a small subset of the compounds described therein, and (iv) Inaba provides no reason for a person of ordinary skill in the art to prepare the compounds of the present invention.



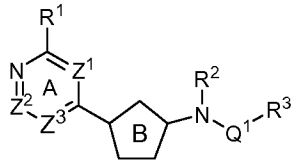
Inaba compound 51



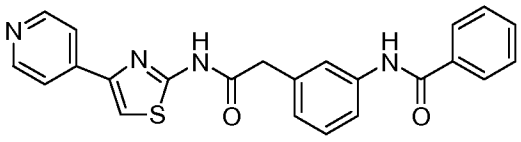
Inaba compound 80

Only 7 (2%) of the 306 compounds that are exemplified in Inaba have a pyridyl substituent at the position corresponding to the Ring A pyridin-4-yl substituent of the compounds of the present invention. See below for the structure of compounds of formula I. See also compounds 44, 46, 51, 80, 82, 113, and 114 on pages 34 to 110 of Inaba. Biological data are presented for only 2 of these 7 compounds (compounds 44 and 113, see below for structures) and the data demonstrate that these two compounds are inferior enzyme inhibitors compared to the vast majority of the other compounds of Inaba

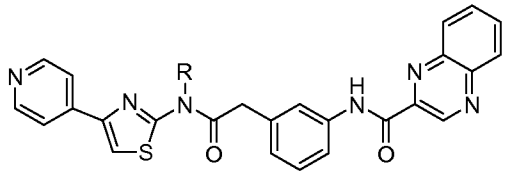
for which similar data are reported. See Tables 79 to 90 on pages 112 to 123 of Inaba. For example, of the 246 Inaba compounds for which PKC IC_{50} data are reported, 222 compounds (90%) have activity that is more potent than compound 44 against any one of the tested isoforms (PKC-α, PKC-βII, and PKC-γ).



formula I



Inaba compound 44



Inaba compound 113 (R is H)

The Manual of Patent Examination Procedure (MPEP) states that "[h]omology and isomerism involve close structural similarity which must be considered with all other relevant facts in determining the issue of obviousness" and that these factors "should not be automatically equated with *prima facie* obviousness because the claimed invention and the prior art must each be viewed 'as a whole.'" See MPEP § 2144.09 (II). See also MPEP § 2141.02, which states that "[a]scertaining the differences between the prior art and the claims at issue requires interpreting the claim language, and considering both the invention and the prior art references as a whole" (emphasis added). The specific compounds of Inaba cited by the Examiner in his obviousness rejection represent a small sub-genus of the compounds described therein and are not reflective of the Inaba reference as a whole. Further, no biological activity was reported in Inaba for cited compounds 51 and 80. Further still, the only biological activity data by Inaba for pyridinyl thiazole compounds indicate that these compounds are inferior kinase inhibitors

compared to the vast majority of the other compounds described therein, thus teaching away from the preparation or use of pyridinyl thiazoles as kinase inhibitors. By focusing in on a narrow sub-genus of compounds in Inaba, the Examiner failed to accurately assess the scope and content of the prior art.

Scope and content of the prior art relating to compound use was not properly established

The Examiner also failed to correlate the uses of the compounds described in Inaba to those of the present invention. In the November Office Action, the Examiner stated that Inaba describes compounds that are useful for the treatment of Alzheimer's disease or allergy. In response, applicants stated that they were unable to find the relevant descriptive text in Inaba that relates to the treatment of these diseases by the compounds described therein and provided a Chemical Abstracts Service abstract indicating that the compounds of Inaba were prepared as sedatives. It was also pointed out to the Examiner that, according to the Manual of Patent Examining Procedure (MPEP) § 707.07, "[i]n citing foreign published applications or patents, in case only a part of the document is involved, the particular pages and sheets containing the parts relied upon will be identified."). As part of the Final Office Action, the Examiner provided a Japanese-to-English machine translation of Inaba in its entirety (provided herein in the Evidence Appendix), but failed to point to that part of Inaba that demonstrates that *the compounds described therein* are useful for the treatment of Alzheimer's disease or allergy.

As seen in the machine-translated copy of Inaba, the background information provided in paragraph [0002] describes PKC as a serine/threoine protein kinase that plays a central role in various intracellular signal transduction processes. Paragraph [0003] of Inaba then speculates that a plethora of diseases can be checked by compounds that moderate PKC activity. These diseases include diabetic complications, arteriosclerosis, angiopathy, inflammation (thrombosis), dermatosis, immune diseases, central nervous

system diseases (e.g., Alzheimer's Disease), and cancer. It is clear from paragraphs [0004] and [0005] of Inaba, however, that *the compounds described therein* are not directed to the many diseases mentioned in the background section but instead to the amelioration of pain. Further, the compounds of Inaba purportedly solve this problem via the selective inhibition of PKC-gamma protein kinase, whilst introductory paragraphs [0002] and [0003] of Inaba relate to general PKC kinase activity. By not identifying a section of Inaba that describes the use of the compounds described therein, the Examiner did not properly establish the scope and content of the prior art related to use.

The prior art did not suggest a finite number of predictable solutions

In addition to the guidance provided in the MPEP regarding Graham discussed above, the law as held in Proctor & Gamble Co. v. Teva Pharmaceuticals Inc., (Fed. Cir. 2009), citing Takeda Chem. Indus., Ltd. V. Alphapharm Pty., Ltd., 492 F.3d 1350, 1357 (Fed. Cir. 2007), makes it clear that an obviousness rejection in the chemical arts based on a structural similarity between claimed and a prior art compound "depends on a preliminary finding that one of ordinary skill in the art would have selected [the prior art compound] as a lead compound." See also Eisai Co. Ltd. V. Dr. Reddy's Labs., Ltd., 533 F.3d 1353, 1359 (Fed. Cir. 2008) which states that "a prima facie case of obviousness for a chemical compound still, in general, begins with the reasoned identification of a lead compound" in the prior art. As shown above, the cited pyridyl thiazole compounds of Inaba are inferior enzyme inhibitors when compared to the vast majority of the other compounds contained in this reference. Further, the Examiner did not provide a reason why any of the pyridyl thiazole compounds identified in Inaba would serve as a starting point in the preparation of the compounds of the present invention.

Conclusion

The Examiner has failed to make a *prima facie* case of obviousness in his rejection of claims 1, 4, 5, 8-12, 14-20, 23-29, 31, 33-46, and 54-57 over Inaba. The scope and content of the prior art and differences between the claims and the prior art were not properly established as required by Graham because (i) the Examiner focused on a narrow subset of prior art compounds that possessed no extraordinary activity and (ii) the Examiner did not correlate the use of the compounds of the prior art to those of the present invention. In addition, the Examiner did not present a reasoned case why a skilled person would select any of the cited compounds of Inaba as a lead compound for the preparation of the compounds of the present invention. Failing to do so indicates that the prior art does not present a finite number of identified predictable solutions that a person of reasonable skills would pursue as required by KSR. Therefore, applicants respectfully request that the obviousness rejection under 35 U.S.C. § 103(a) be withdrawn and the claims allowed to pass to issue.

Respectfully submitted,

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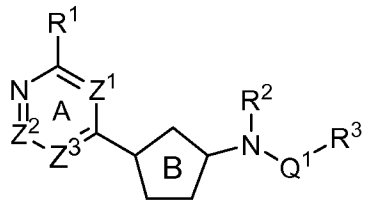
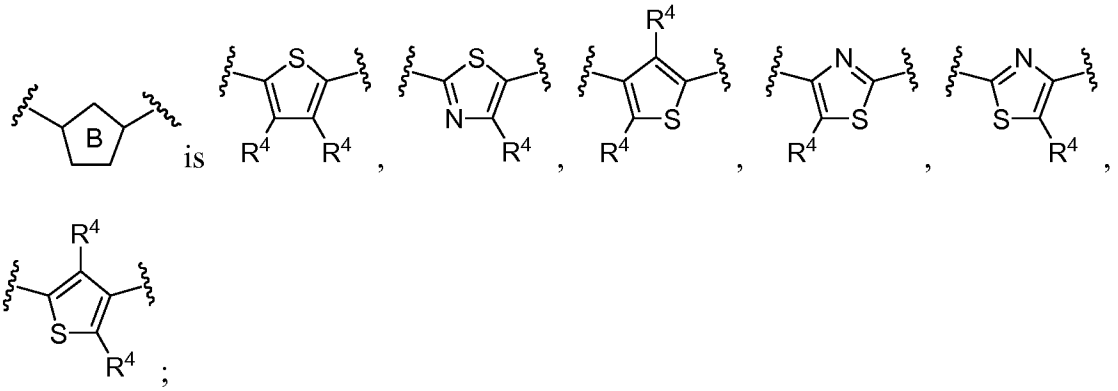
CLAIMS APPENDIX

1. A compound of formula **I**:



I

or a pharmaceutically acceptable salt thereof, wherein:



is , , , , , or ;

R^1 is halogen, CN, NO_2, or V_mR;

Z^1 and Z^3 are each independently CR^Z;

Z^2 is CR^1;

each occurrence of R^Z is independently halogen, CN, NO_2, or U_nR';

R^2 is U_nR';

each occurrence of R^4 is independently halogen, CN, NO_2, or V_mR;

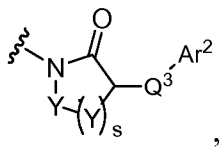
each occurrence of U or V is independently an optionally substituted C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by -NR-, -S-, -O-, -CS-, -OCO-, -COCO-, -CONR-, -NRCO-, -$NRCO_2$-, -SO_2NR-, -$NRSO_2$-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -$NRSO_2NR$-, -SO-, or -SO_2-;

m and n are each independently 0 or 1;

each occurrence of R is independently hydrogen or an optionally substituted C_{1-6} aliphatic group; and each occurrence of R′ is independently hydrogen or an optionally substituted C_{1-6} aliphatic group, or a 3-8-membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or R and R′, two occurrences of R, or two occurrences of R′, are taken together with the atom(s) to which they are bound to form an optionally substituted 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Q^1 is -CO-;

R^3 is Q^2-Ar^1, wherein Q^2 is -$(CHR^6)_q$-, where q is 1, 2, or 3,

or R^2 and Q^1-R^3, taken together with the intervening nitrogen atom, form the cyclic group:  , where s is 1 or 2, each occurrence of Y is independently, as

valency and stability permit, -CO-, -CS-, -SO_2-, -O-, -S-, -NR^5-, or -$C(R^5)_2$-, and R^5 is U_nR';

Q^3 is a bond or a C_{1-6} alkylidene chain, wherein up to two methylene units of the chain are each optionally and independently replaced by -S-, -O-, -CS-, -CO_2-, -OCO-, -CO-, -COCO-, -CONR′-, -NR′CO-, -NR′CO_2-, -SO_2NR′-, -NR′SO_2-, -CONR′NR′-, -NR′CONR′-, -OCONR′-, -NR′NR′-, -NR′SO_2NR′-, -SO-, or -SO_2-; and wherein any carbon atom in the one or more methylene units is optionally substituted with one or two occurrences of R^6, wherein each occurrence of R^6 is independently halogen, CN, NO_2, or U_nR', or two occurrences of R^6, or R′ and R^6, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered cycloalkyl, heterocyclyl, aryl or heteroaryl ring; and

Ar^1 is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from oxygen or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from oxygen or sulfur; wherein Ar^1 is optionally substituted with 0-5 independent occurrences of TR^7; wherein T is a bond or is a C_1-C_6 alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by -NR-, -S-, -O-, -CS-, -CO_2-, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, -NRCO_2-, -SO_2NR-, -NRSO_2-, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, -NRSO_2NR-, -SO-, or -SO_2-;

Ar^2 is a 5-8 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; wherein Ar^2 is optionally substituted with 0-5 independent occurrences of TR^7; wherein T is a bond or is a C_1-C_6 alkylidene chain wherein up to two methylene units of T are optionally and independently replaced by -NR-, -S-, -O-, -CS-, $-CO_2-$, -OCO-, -CO-, -COCO-, -CONR-, -NRCO-, $-NRCO_2-$, $-SO_2NR-$, $-NRSO_2-$, -CONRNR-, -NRCONR-, -OCONR-, -NRNR-, $-NRSO_2NR-$, -SO-, or $-SO_2-$;

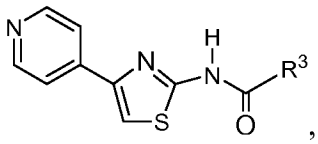
each occurrence of R^7 is independently R′, halogen, NO_2, or CN;

each of the optional substituents of said aryl or heteroaryl ring is selected from halogen; -R°; -OR°; -SR°; phenyl optionally substituted with R^o; -O(phenyl), optionally substituted with R^o; $-(CH_2)_{1-2}$(phenyl), optionally substituted with R^o; -CH=CH(phenyl), optionally substituted with R^o; $-NO_2$; -CN; $-N(R°)_2$; -NR°C(O)R°; -NR°C(S)R°; $-NR°C(O)N(R°)_2$; $-NR°C(S)N(R°)_2$; $-NR°CO_2R°$; -NR°NR°C(O)R°; $-NR°NR°C(O)N(R°)_2$; $-NR°NR°CO_2R°$; -C(O)C(O)R°; $-C(O)CH_2C(O)R°$; $-CO_2R°$; -C(O)R°; -C(S)R°; $-C(O)N(R°)_2$; $-C(S)N(R°)_2$; $-OC(O)N(R°)_2$; -OC(O)R°; -C(O)N(OR°)R°; -C(NOR°) R°; $-S(O)_2R°$; $-S(O)_3R°$; $-SO_2N(R°)_2$; -S(O)R°; $-NR°SO_2N(R°)_2$; $-NR°SO_2R°$; -N(OR°)R°; $-C(=NH)-N(R°)_2$; $-P(O)_2R°$; $-PO(R°)_2$; $-OPO(R°)_2$; $-(CH_2)_{0-2}NHC(O)R°$; wherein each independent occurrence of R° is selected

from hydrogen, an optionally substituted C_{1-6} aliphatic, an unsubstituted 5-6 membered heteroaryl or heterocyclic ring, phenyl, -O(phenyl), or -CH_2(phenyl), wherein optional substituents on the aliphatic group of R° are selected from NH_2, NH(C_{1-4}aliphatic), N(C_{1-4}aliphatic)$_2$, halogen, C_{1-4}aliphatic, OH, O(C_{1-4}aliphatic), NO_2, CN, CO_2H, CO_2(C_{1-4}aliphatic), O(haloC_{1-4} aliphatic), or haloC_{1-4}aliphatic, or two independent occurrences of R°, on the same substituent or different substituents, taken together with the atom(s) to which each R° group is bound, form a 3-12 membered saturated, partially unsaturated, or fully unsaturated monocyclic or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and

each of the optional substituents on said alkylidene chain, aliphatic, cycloalkyl, or heterocyclyl is selected from the list of optional substituents of optional substituents for aryl and heteroaryl rings and further comprise =O, =S, =NNHR*, =NN(R*)$_2$, =NNHC(O)R*, =NNHCO$_2$(alkyl), =NNHSO$_2$(alkyl), or =NR*, where each R* is independently selected from hydrogen or a C_{1-6} aliphatic group;

provided that:

for compounds having the structure: 

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R^3 is not any one of the following groups: -CH_2(3-NHCOPh-phenyl), -CH_2-pyrrolidine, unsubstituted benzyl, -CH_2-naphthyl, -CH_2CH_2-3-(4-Cl-phenyl)-1-phenyl-1-H-pyrazol-4-yl, or -CH_2(1,3-dioxoisoindole).

2-3. (Canceled)

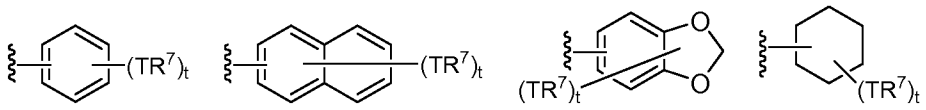
4. The compound of claim 1, wherein R^2 is hydrogen, or is U_nR', where n is 1, and U is a C_{1-6} alkylidene chain wherein one or two methylene units are optionally and independently replaced by O, NR, S, or C(O).

5. The compound of claim 1, wherein U is $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, $-CH_2O-$, $-CH_2S-$, $-CH_2NR-$, $-CH_2CH_2O-$, $-CH_2CH_2S-$, $-CH_2CH_2NR-$, $-CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2S-$, $-CH_2CH_2CH_2NR-$, $-CH_2CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2CH_2S-$, $-CH_2CH_2CH_2CH_2NR-$, $-CH_2CH_2OCH_2CH_2-$, $-(CH_2)_4NHCH_2-$, $-(CH_2)_3NHCH_2CH_2-$, or $-CH_2CH_2NHCH_2CH_2-$, and preferred R′ groups are hydrogen, C_1-C_4alkyl, optionally substituted tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyridinyl, phenyl, or cyclohexyl, or R and R′, taken together with the nitrogen atom to which they are bound, form an optionally substituted 5- or 6-membered heterocyclyl ring.

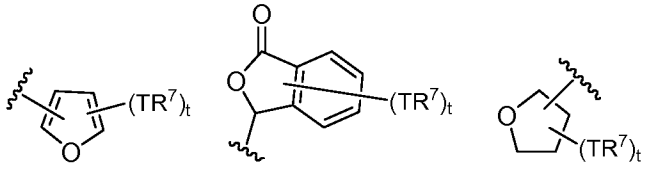
6-7. (Canceled)

8. The compound of claim 1, wherein R^6 is CH_2OH, CH_2CH_2OH, OH, OMe, OEt, NH_2, NH(Me), NH(Et), N(Me)(Me), CH_2NH_2, $CH_2CH_2NH_2$, $NHCO_2t$-butyl, phenyl, cyclopentyl, methyl, ethyl, isopropyl, cyclopropyl, $NH(CH_2)_3NH_2$, $NH(CH_2)_2NH_2$, $NH(CH_2)_2NHEt$, $NHCH_2$pyridyl, $NHSO_2$phenyl, $NHC(O)CH_2C(O)Ot$-butyl, $NHC(O)CH_2NH_3$, and $NHCH_2$-imidazol-4-yl.

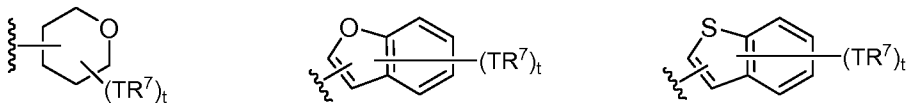
9. The compound of claim 3, wherein Ar^1 is:



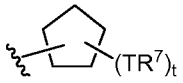
a **e** **i** **k**



t **cc** **ee**



ii **jj** **kk**



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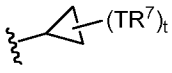

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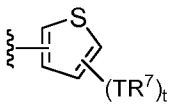


pp

wherein t is 0, 1, 2, 3, 4 or 5, and wherein any Ar^1 is bonded to Q^2 through any substitutable carbon atom, and wherein one or more hydrogen atoms on any substitutable carbon atom is substituted with one or more independent occurrences of TR^7.

10. The compound of claim 9, wherein Ar^1 is **a, e, i, k, cc, jj,** or **pp**.

11. The compound of claim 9, wherein T is a bond or is an optionally substituted C_{1-6} alkylidene chain wherein one or two methylene units are optionally and independently replaced by -O-, -NR-, -S-, $-SO_2-$, -COO-, -CO-, $-OSO_2-$, $-NRSO_2$, -CONR-, or $-SO_2NR-$, and R^7 is R′ or halogen.

12. The compound of claim 9, wherein each occurrence of TR^7 is independently $-C_{1-3}$alkyl, -OR′, -SR′, $-CF_3$, $-OCF_3$, $-SCF_3$, -F, -Cl, I, -Br, -COOR′, -COR′, $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)N(R)(R')$, $-O(CH_2)_4CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)CON(R)(R')$, -C(O)N(R)(R′), $-(CH_2)_4OR'$, $-(CH_2)_3OR'$, $-(CH_2)_2OR'$, $-CH_2OR'$, optionally substituted phenyl or benzyl, -N(R)(R′), $-(CH_2)_4N(R)(R')$,

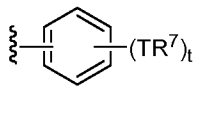
$-(CH_2)_3N(R)(R')$, $-(CH_2)_2N(R)(R')$, $-(CH_2)N(R)(R')$, or $SO_2N(R)(R')$, $NRSO_2R'$, $CON(R)(R')$, or $-OSO_2R'$.

13. (Canceled)

14. The compound of claim 1, wherein Q^3 is a direct bond, or is $-(CHR^6)_q-$, $-(CHR^6)_qO-$, $-(CHR^6)_qS-$, $-(CHR^6)_qS(O)_2-$, $-(CHR^6)_qS(O)-$, $-(CHR^6)_qNR-$, or $-(CHR^6)_qC(O)-$, wherein q is 0, 1, 2, or 3, and R^6 is R′, -N(R)(R′), $-(CH_2)_{1-4}N(R)(R')$, -OR′, $-(CH_2)_{1-4}OR'$, $-NR(CH_2)_{1-4}N(R)(R')$, $-NR(CH_2)_{1-4}SO_2R'$, $-NR(CH_2)_{1-4}COOR'$, or $-NR(CH_2)_{1-4}COR'$, or two occurrences of R^6, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered saturated, partially unsaturated, or fully unsaturated ring.

15. The compound of claim 14, wherein R^6 is CH_2OH, CH_2CH_2OH, OH, OMe, OEt, NH_2, NH(Me), NH(Et), N(Me)(Me), CH_2NH_2, $CH_2CH_2NH_2$, $NHCO_2t$-butyl, phenyl, cyclopentyl, methyl, ethyl, isopropyl, cyclopropyl, $NH(CH_2)_3NH_2$, $NH(CH_2)_2NH_2$, $NH(CH_2)_2NHEt$, $NHCH_2$pyridyl, $NHSO_2$phenyl, $NHC(O)CH_2C(O)Ot$-butyl, $NHC(O)CH_2NH_3$, and $NHCH_2$-imidazol-4-yl.

16. The compound of claim 1, wherein Ar^2 is:



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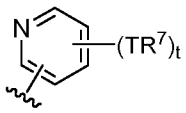

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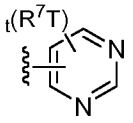

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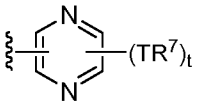

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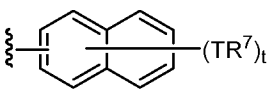

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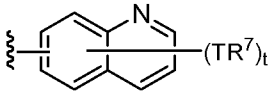

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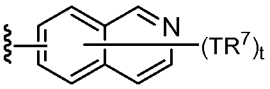

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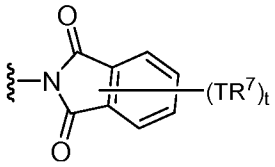

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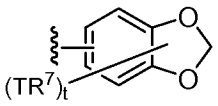

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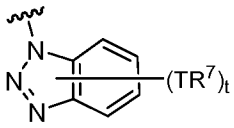

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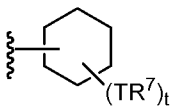

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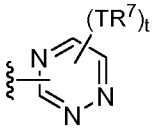

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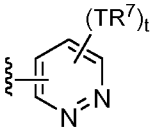

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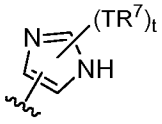

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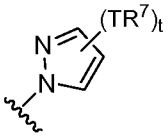

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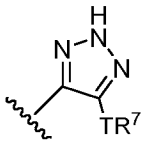

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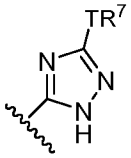

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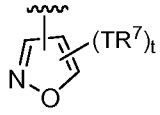

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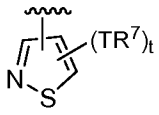

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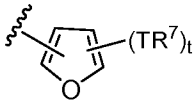

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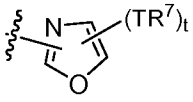

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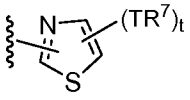

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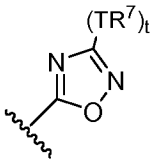

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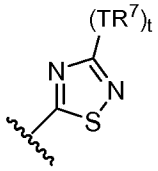

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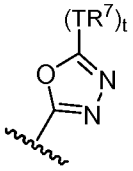

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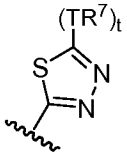

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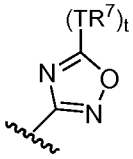

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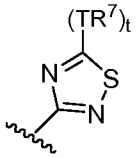

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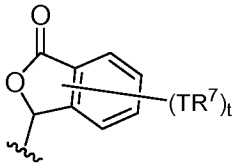

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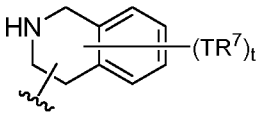

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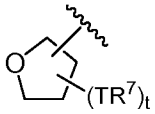

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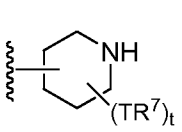

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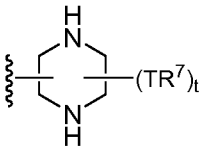

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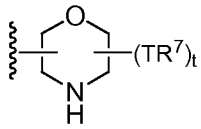

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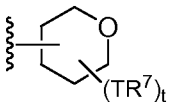

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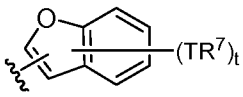

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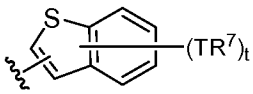

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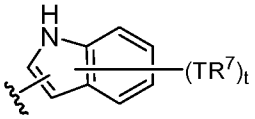

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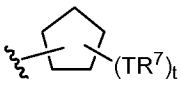

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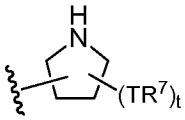

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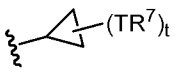

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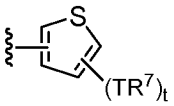


pp

wherein t is 0, 1, 2, 3, 4 or 5, and wherein any Ar^2 is bonded to Q^3 through any substitutable nitrogen or carbon atom, and wherein one or more hydrogen atoms on any substitutable nitrogen or carbon atom is substituted with one or more independent occurrences of TR^7.

17. The compound of claim 16, wherein Ar^2 is **a, b, e, g, h, i, j, k, n, r, cc, dd, ff, jj, ll**, or **pp**.

18. The compound of claim 16, wherein T is a bond or is an optionally substituted C_{1-6} alkylidene chain wherein one or two methylene units are optionally and independently replaced by -O-, -NR-, -S-, $-SO_2-$, -COO-, -CO-, $-OSO_2-$, $-NRSO_2$, -CONR-, or $-SO_2NR-$, and R^7 is R′ or halogen.

19. The compound of claim 16, wherein each occurrence of TR^7 is independently $-C_{1-3}$alkyl, -OR′, -SR′, $-CF_3$, $-OCF_3$, $-SCF_3$, -F, -Cl, I, -Br, -COOR′, -COR′, $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)N(R)(R')$, $-O(CH_2)_4CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)CON(R)(R')$, -C(O)N(R)(R′), $-(CH_2)_4OR'$, $-(CH_2)_3OR'$, $-(CH_2)_2OR'$, $-CH_2OR'$, optionally substituted phenyl or benzyl, -N(R)(R′), $-(CH_2)_4N(R)(R')$, $-(CH_2)_3N(R)(R')$, $-(CH_2)_2N(R)(R')$, $-(CH_2)N(R)(R')$, or $SO_2N(R)(R')$, $NRSO_2R'$, CON(R)(R′), or $-OSO_2R'$.

20. The compound of claim 1, wherein R^5 is hydrogen, $(CH_2)_3OR'$, $(CH_2)_2OR'$, $(CH_2)OR'$, $(CH_2)_3N(R')_2$, $(CH_2)_2N(R')_2$, $(CH_2)N(R')_2$, or C_{1-4}aliphatic.

21-22. (Canceled)

23. The compound of claim 1, wherein each occurrence of R^1 is independently hydrogen, halogen, optionally substituted C_1-C_4aliphatic, OR, SR, or $N(R)_2$.

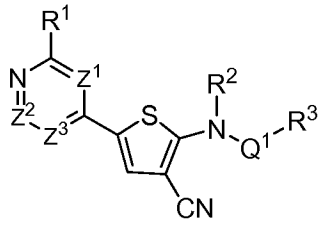
24. The compound of claim 23, wherein each occurrence of R^1 is independently hydrogen, halogen, $-CH_3$, $-CH_2CH_3$, -OH, $-OCH_3$, $-SCH_3$, $-NH_2$, $-N(CH_3)_2$, $-N(CH_2CH_3)_2$, $-NH(CH_2)_2NHCH_3$, -NH(cyclopropyl), $-NH(CH_2)$cyclopropyl, or $-NH(CH_2)_2N(CH_3)_2$.

25. The compound of claim 1, wherein each occurrence of R^Z is independently hydrogen, halogen, C_1-C_4aliphatic, OH, OR′, or N(R)(R′).

26. The compound of claim 25, wherein each occurrence of R^Z is independently hydrogen, halogen, Me, OH, OMe, NH_2, or $N(Me)_2$.

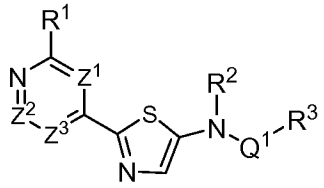
27. The compound of claim 1, wherein R^4 groups are each independently hydrogen, C_{1-6}aliphatic, CN, $C(=O)N(R)_2$, or halogen.

28. The compound of claim 1, wherein one occurrence of R^4 is CN and compounds have the general structure **II-a**:



II-a.

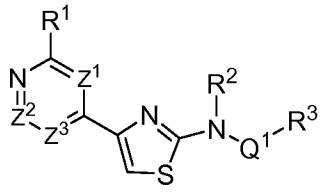
29. The compound of claim 1, wherein R^4 is hydrogen and compounds have the general structure **III-a**:



III-a.

30. (Canceled)

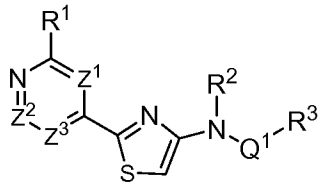
31. The compound of claim 1, wherein R^4 is hydrogen and compounds have the general structure **VII-a**:



VII-a.

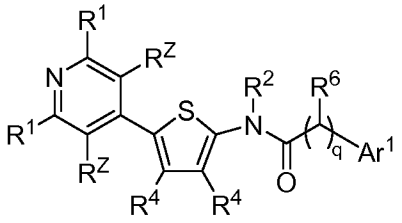
32. (Canceled)

33. The compound of claim 1, wherein R^4 is hydrogen and compounds have the general structure **XI-a**:

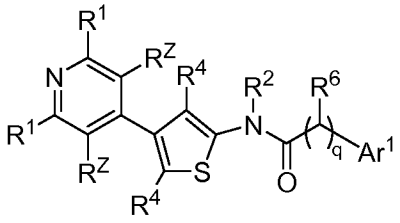


XI-a.

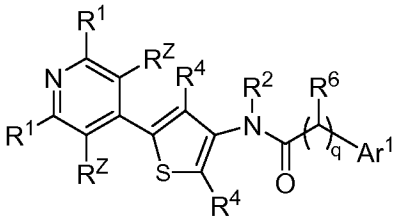
34. The compound of claim 9, wherein Q^1 is -CO-, Q^2 is CHR^6, q is 1 2, or 3, and compounds have one of formulas **XIV, XV,** or **XVI:**



XIV

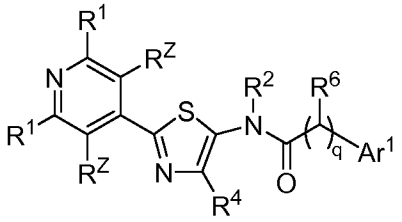


XV

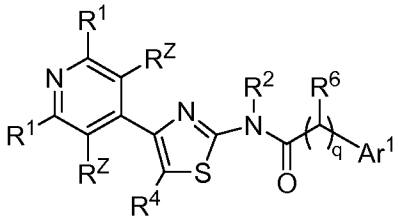


XVI.

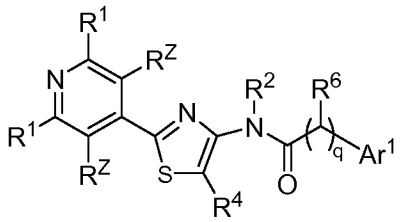
35. The compound of claim 9, wherein Q^1 is -CO-, Q^2 is CHR^6, q is 1, 2 or 3, and compounds have one of formulas **XVII, XVIII,** or **XIX:**



XVII



XVIII



XIX.

36. The compound of claims 34 or 35, wherein compound variables are selected from one of more of the following groups:

a) each occurrence of R^1 is independently hydrogen, halogen, optionally substituted C_1-C_4aliphatic, OR, SR, or $N(R)_2$;

b) each occurrence of R^1 is independently hydrogen, halogen, $-CH_3$, $-CH_2CH_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-NH_2$, $-N(CH_3)_2$, $-N(CH_2CH_3)_2$, $-NH(CH_2)_2NHCH_3$, $-NH$(cyclopropyl), $-NH(CH_2)$cyclopropyl, or $-NH(CH_2)_2N(CH_3)_2$;

c) each occurrence of R^Z is independently hydrogen, halogen, optionally substituted C_1-C_4aliphatic, OH, O(R′), or N(R)(R′);

d) each occurrence of R^Z is independently hydrogen, halogen, Me, OH, OMe, NH_2, or $N(Me)_2$;

e) R^2 is hydrogen, or is U_nR', where n is 1, and U is–CH_2-, $-CH_2CH_2$-, $-CH_2CH_2CH_2$-, $-CH_2CH_2CH_2CH_2$-, $-CH_2O$-, $-CH_2S$-, $-CH_2NR$-, $-CH_2CH_2O$-, $-CH_2CH_2S$-, $-CH_2CH_2NR$-, $-CH_2CH_2CH_2O$-, $-CH_2CH_2CH_2S$-, $-CH_2CH_2CH_2NR$-, $-CH_2CH_2CH_2CH_2O$-, $-CH_2CH_2CH_2CH_2S$-, $-CH_2CH_2CH_2CH_2NR$-,

$-CH_2CH_2OCH_2CH_2-$, $-(CH_2)_4NHCH_2-$, $-(CH_2)_3NHCH_2CH_2-$, or $-CH_2CH_2NHCH_2CH_2-$, and R′ groups are hydrogen, C_1-C_4alkyl, optionally substituted tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyridinyl, phenyl, or cyclohexyl, or R and R′, taken together with the nitrogen atom to which they are bound, form an optionally substituted 5- or 6-membered heterocyclyl ring;

f) each occurrence of R^4 is independently hydrogen, C_{1-6}aliphatic, CN, COR, COOR, $CON(R)_2$, or halogen;

g) q is 1, 2, or 3;

h) R^6 is R′, -N(R)(R′), $-(CH_2)_{1-4}N(R)(R')$, -OR′, $-(CH_2)_{1-4}OR'$, $-NR(CH_2)_{1-4}N(R)(R')$, $-NR(CH_2)_{1-4}SO_2R'$, $-NR(CH_2)_{1-4}COOR'$, or $-NR(CH_2)_{1-4}COR'$, or two occurrences of R^6, taken together with the atoms to which they are bound, form an optionally substituted 3-6-membered saturated, partially unsaturated, or fully unsaturated ring;

i) R^6 is CH_2OH, CH_2CH_2OH, OH, OMe, OEt, NH_2, NH(Me), NH(Et), N(Me)(Me), CH_2NH_2, $CH_2CH_2NH_2$, $NHCO_2t$-butyl, phenyl, cyclopentyl, methyl, ethyl, isopropyl, cyclopropyl, $NH(CH_2)_3NH_2$, $NH(CH_2)_2NH_2$, $NH(CH_2)_2NHEt$, $NHCH_2$pyridyl, $NHSO_2$phenyl, $NHC(O)CH_2C(O)Ot$-butyl, $NHC(O)CH_2NH_3$, and $NHCH_2$-imidazol-4-yl;

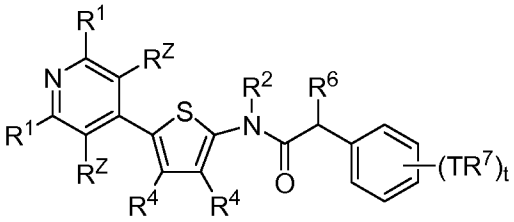
j) Ar^1 is ring **a, e, i, k, cc, jj,** or **pp** wherein t is 0, 1, 2, or 3, and T is a bond or is an optionally substituted C_{1-6} alkylidene chain wherein one or two methylene units are

optionally and independently replaced by -O-, -NR-, -S-, -SO_2-, -COO-, -CO-, -OSO_2-, -$NRSO_2$, -CONR-, or

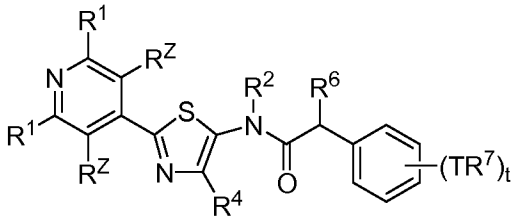
-SO_2NR-, and R^7 is R′ or halogen; or

k) Ar^1 is ring **a, e, i, k, cc, jj,** or **pp** wherein t is 0, 1, 2, or 3, and each occurrence of TR^7 is independently -C_{1-3}alkyl, -OR′, -SR′, -CF_3, -OCF_3, -SCF_3, -F, -Cl, I, -Br, -COOR′, -COR′, -$O(CH_2)_4N(R)(R')$, -$O(CH_2)_3N(R)(R')$, -$O(CH_2)_2N(R)(R')$, -$O(CH_2)N(R)(R')$, -$O(CH_2)_4CON(R)(R')$, -$O(CH_2)_3CON(R)(R')$, -$O(CH_2)_2CON(R)(R')$, -$O(CH_2)CON(R)(R')$, -$C(O)N(R)(R')$, -$(CH_2)_4OR'$, -$(CH_2)_3OR'$, -$(CH_2)_2OR'$, -CH_2OR', optionally substituted phenyl or benzyl, -$N(R)(R')$, -$(CH_2)_4N(R)(R')$, -$(CH_2)_3N(R)(R')$, -$(CH_2)_2N(R)(R')$, -$(CH_2)N(R)(R')$, -$SO_2N(R)(R')$, -$NRSO_2R'$, -$CON(R)(R')$, or -OSO_2R'.

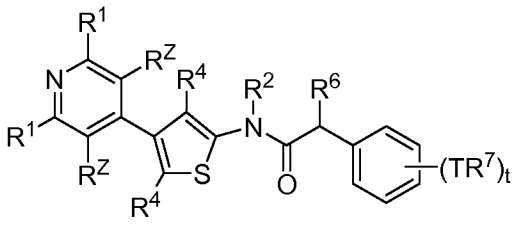
37. The compound of claim 34 or 35, q is 1, and Ar^1 is optionally substituted phenyl and compounds of general formula **XIV-A** through **XIX-A** are provided:



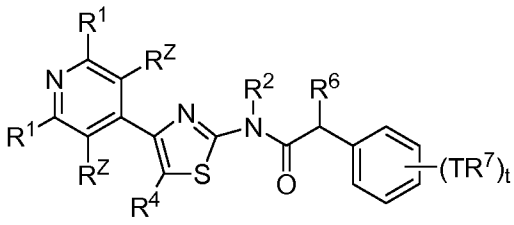
XIV-A



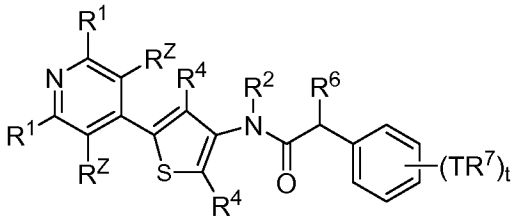
XV-A



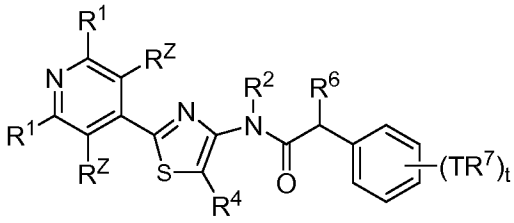
XVI-A



XVII-A



XVIII-A



XIX-A

wherein:

each occurrence of R^1 is hydrogen;

each occurrence of R^Z is hydrogen;

R^2 is hydrogen, or is U_nR', where n is 1, and U is $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, $-CH_2O-$, $-CH_2S-$, $-CH_2NR-$, $-CH_2CH_2O-$, $-CH_2CH_2S-$, $-CH_2CH_2NR-$, $-CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2S-$, $-CH_2CH_2CH_2NR-$, $-CH_2CH_2CH_2CH_2O-$, $-CH_2CH_2CH_2CH_2S-$, $-CH_2CH_2CH_2CH_2NR-$, $-CH_2CH_2OCH_2CH_2-$, $-(CH_2)_4NHCH_2-$, $-(CH_2)_3NHCH_2CH_2-$, or $-CH_2CH_2NHCH_2CH_2-$, and R′ groups are hydrogen, C_1-C_4alkyl, optionally substituted tetrahydropyranyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyridinyl, phenyl, or cyclohexyl, or R and R′,

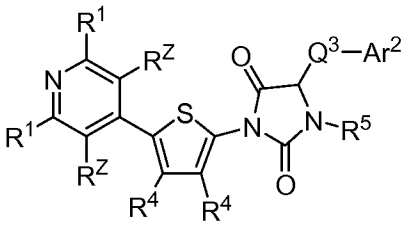
taken together with the nitrogen atom to which they are bound, form an optionally substituted 5- or 6-membered heterocyclyl ring;

each occurrence of R^4 is independently hydrogen, C_{1-6}aliphatic, CN, $CON(R)_2$, or halogen;

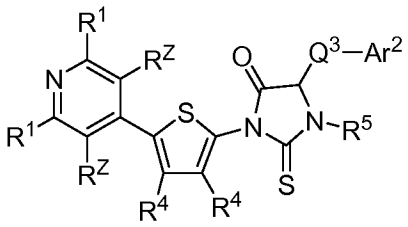
R^6 is R′, -N(R)(R′), $-(CH_2)_{1-4}N(R)(R')$, -OR′, $-(CH_2)_{1-4}OR'$, $-NR(CH_2)_{1-4}N(R)(R')$, $-NR(CH_2)_{1-4}SO_2R'$, $-NR(CH_2)_{1-4}COOR'$, or $-NR(CH_2)_{1-4}COR'$; and

t is 0, 1, 2, or 3, and each occurrence of TR^7 is independently $-C_{1-3}$alkyl, -OR′, -SR′, $-CF_3$, $-OCF_3$, $-SCF_3$, -F, -Cl, I, -Br, -COOR′, -COR′, $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)N(R)(R')$, $-O(CH_2)_4CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)CON(R)(R')$, -C(O)N(R)(R′), $-(CH_2)_4OR'$, $-(CH_2)_3OR'$, $-(CH_2)_2OR'$, $-CH_2OR'$, optionally substituted phenyl or benzyl, -N(R)(R′), $-(CH_2)_4N(R)(R')$, $-(CH_2)_3N(R)(R')$, $-(CH_2)_2N(R)(R')$, $-(CH_2)N(R)(R')$, $-SO_2N(R)(R')$, $-NRSO_2R'$, -CON(R)(R′), or $-OSO_2R'$.

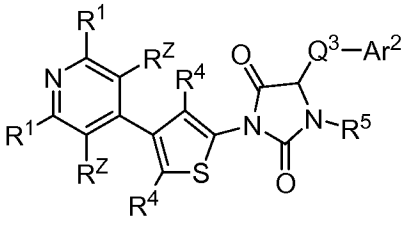
38. The compound of claim 16, wherein R^2 and Q^1-R^3, taken together with the atoms to which they are bound form a 5-membered cyclic group, and compounds have the general formula **XX** through **XXV:**



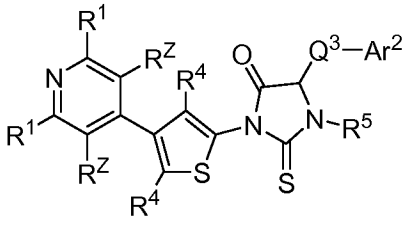
XX



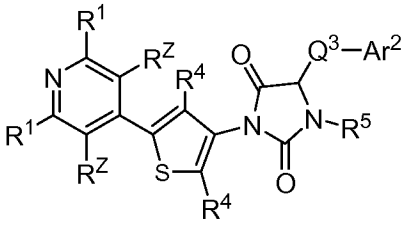
XXI



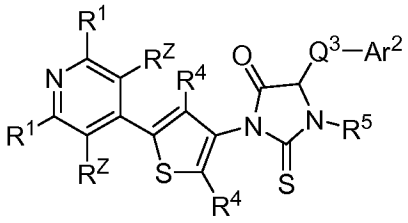
XXII



XXIII

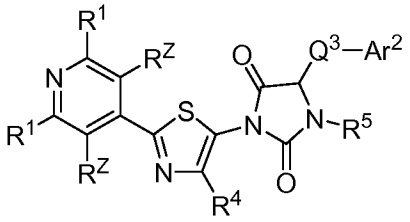


XXIV

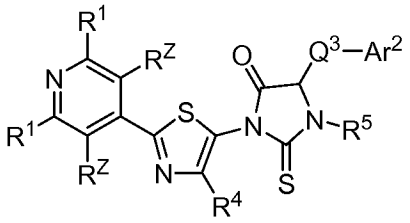


XXV.

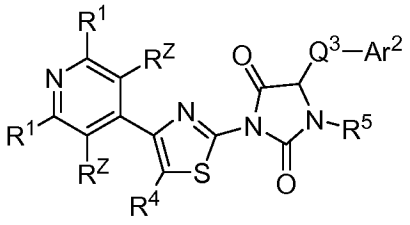
39. The compound of claim 16, R^2 and Q^1-R^3, taken together with the atoms to which they are bound form a 5-membered cyclic group, and compounds have the general formula **XXVI** through **XXXI:**



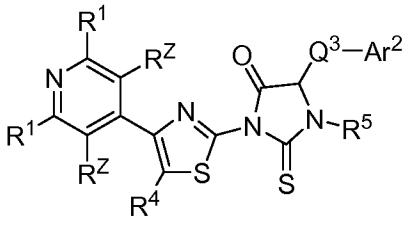
XXVI



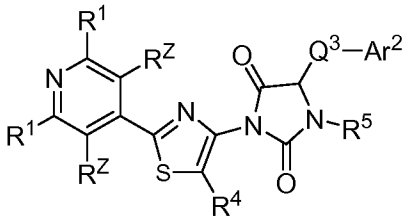
XXVII



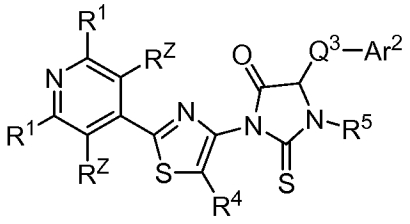
XXVIII



XXIX

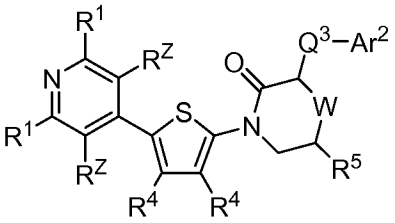


XXX

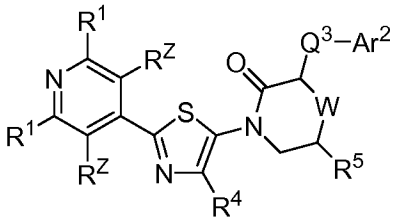


XXXI.

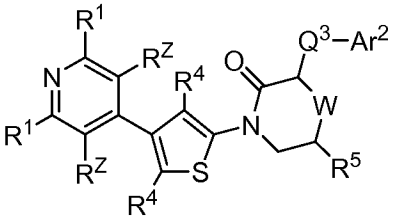
40. The compound of claim 16, wherein R^2 and Q^1-R^3, taken together with the atoms to which they are bound form a 6-membered cyclic group, and compounds have the general formula **XXXII** through **XXXVII:**



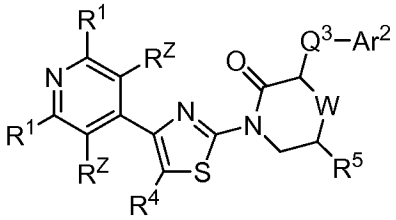
XXXII



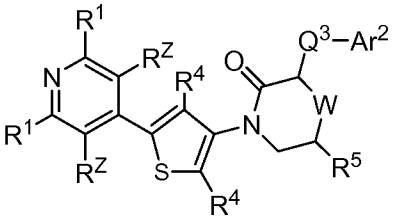
XXXIII



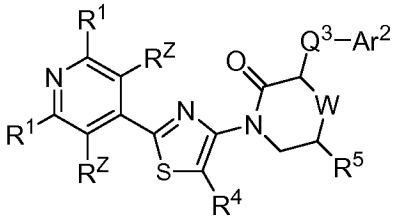
XXXIV



XXXV



XXXVI



XXXVII

wherein W is O, NR^5, or CHR^5.

41. The compound of claims 38, 39 or 40, wherein compound variables are selected from one of more of the following groups:

a) each occurrence of R^1 is independently hydrogen, halogen, optionally substituted C_1-C_4aliphatic, OR, SR, or $N(R)_2$;

b) each occurrence of R^Z is independently hydrogen, halogen, optionally substituted C_1-C_4aliphatic, OH, OR′ or N(R)(R′);

c) each occurrence of R^4 is independently hydrogen, C_{1-6}aliphatic, CN, COR, COOR, $CON(R)_2$, or halogen;

d) R^5 is hydrogen, $(CH_2)_3OR'$, $(CH_2)_2OR'$, $(CH_2)OR'$, $(CH_2)_3N(R')_2$, $(CH_2)_2N(R')_2$, $(CH_2)N(R')_2$, or C_{1-4}aliphatic;

e) Q^3 is a direct bond, or is $-(CHR^6)_q-$, $-(CHR^6)_qO-$, $-(CHR^6)_qS-$, $-(CHR^6)_qS(O)_2-$, $-(CHR^6)_qS(O)-$, $-(CHR^6)_qNR-$, or $-(CHR^6)_qC(O)-$, wherein q is 0, 1, 2, or 3; and

f) Ar^2 is ring **a, b, e, g, h, i, j, k, n, r, cc, dd, ff, jj, ll**, or **pp**, wherein t is 0, 1, 2, or 3, and T is a bond or is an optionally substituted C_{1-6} alkylidene chain wherein one or two methylene units are optionally and independently replaced by –O-, -NR-, -S-, $-SO_2-$, -COO-, -CO-, $-OSO_2-$, $-NRSO_2$, -CONR-, or $-SO_2NR-$, and R^7 is R′ or halogen.

42. The compound of claims 38, 39 or 40, wherein compound variables are selected from one of more of the following groups:

a) each occurrence of R^1 is independently hydrogen, halogen, $-CH_3$, $-CH_2CH_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-NH_2$, $-N(CH_3)_2$, $-N(CH_2CH_3)_2$, $NH(CH_2)_2NHCH_3$, NH(cyclopropyl), $NH(CH_2)$cyclopropyl, or $NH(CH_2)_2N(CH_3)_2$;

b) each occurrence of R^Z is independently hydrogen, halogen, Me, OH, OMe, NH_2, or $N(Me)_2$;

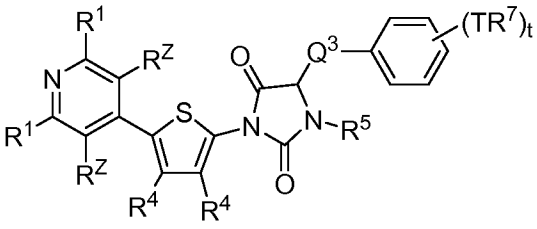
c) each occurrence of R^4 is independently hydrogen, C_{1-6}aliphatic, CN, $CON(R)_2$, or halogen;

d) R^5 is hydrogen, $(CH_2)_3OR'$, $(CH_2)_2OR'$, $(CH_2)OR'$, $(CH_2)_3N(R')_2$, $(CH_2)_2N(R')_2$, $(CH_2)N(R')_2$, or C_{1-4}aliphatic;

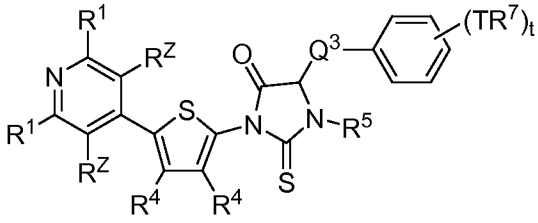
e) Q^3 is a direct bond, or is $-(CHR^6)_q-$, $-(CHR^6)_qO-$, $-(CHR^6)_qS-$, $-(CHR^6)_qS(O)_2-$, $-(CHR^6)_qS(O)-$, $-(CHR^6)_qNR-$, or $-(CHR^6)_qC(O)-$, wherein q is 0, 1, 2, or 3; and

f) Ar^2 is ring **a, b, e, g, h, i, j, k, n, r, cc, dd, ff, jj, ll**, or **pp**, wherein t is 0, 1, 2, or 3, and each occurrence of TR^7 is independently $-C_{1-3}$alkyl, $-OR'$, $-SR'$, $-CF_3$, $-OCF_3$, $-SCF_3$, -F, -Cl, I, -Br, $-COOR'$, $-COR'$, $-O(CH_2)_4N(R)(R')$, $-O(CH_2)_3N(R)(R')$, $-O(CH_2)_2N(R)(R')$, $-O(CH_2)N(R)(R')$, $-O(CH_2)_4CON(R)(R')$, $-O(CH_2)_3CON(R)(R')$, $-O(CH_2)_2CON(R)(R')$, $-O(CH_2)CON(R)(R')$, $-C(O)N(R)(R')$, $-(CH_2)_4OR'$, $-(CH_2)_3OR'$, $-(CH_2)_2OR'$, $-CH_2OR'$, optionally substituted phenyl or benzyl, $-N(R)(R')$, $-(CH_2)_4N(R)(R')$, $-(CH_2)_3N(R)(R')$, $-(CH_2)_2N(R)(R')$, $-(CH_2)N(R)(R')$, $-SO_2N(R)(R')$, $-NRSO_2R'$, $-CON(R)(R')$, or $-OSO_2R'$.

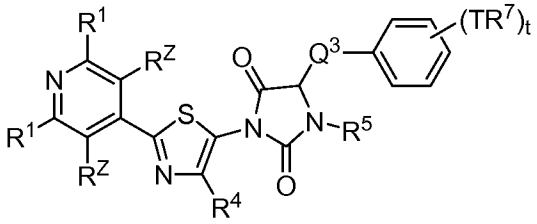
43. The compound of claims 38, 39 or 40, wherein Ar^2 is optionally substituted phenyl and compounds of general formula **XX-A,** through **XXXVII** are provided:



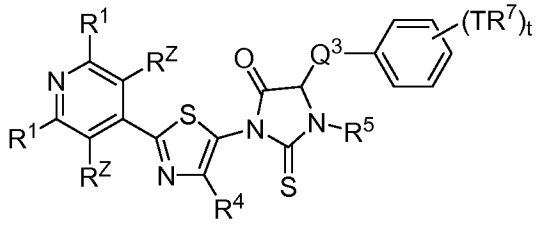
XX-A



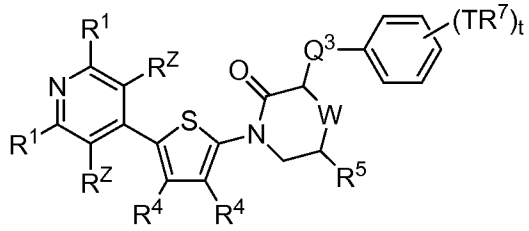
XXI-A



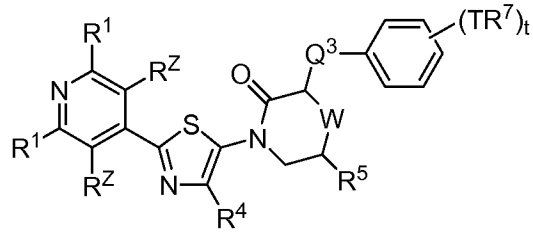
XXII-A



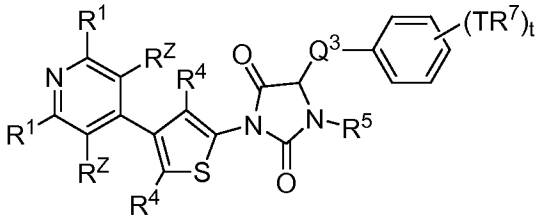
XXIII-A



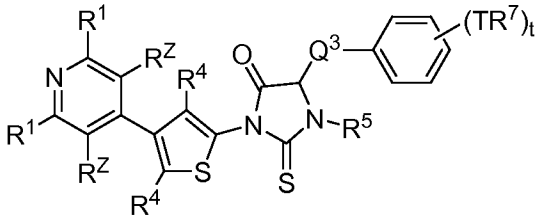
XXIV-A



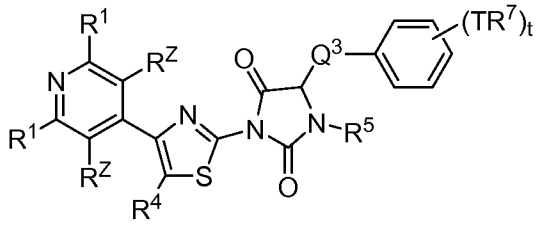
XXV-A



XXVI-A



XXVII-A



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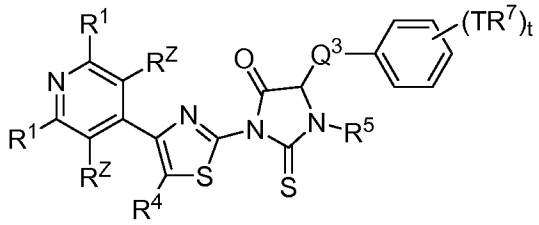
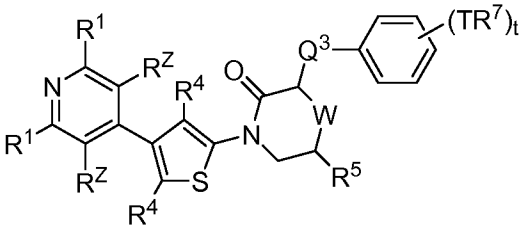
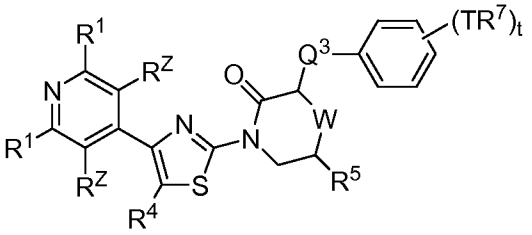


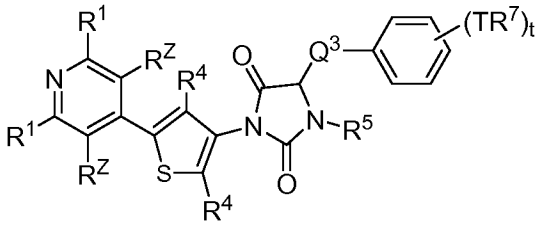
XXIX-A

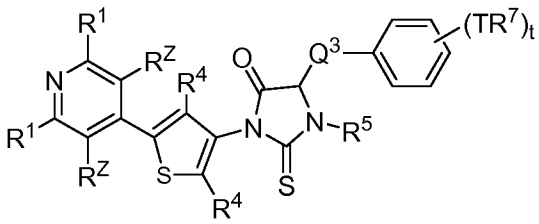


XXX-A

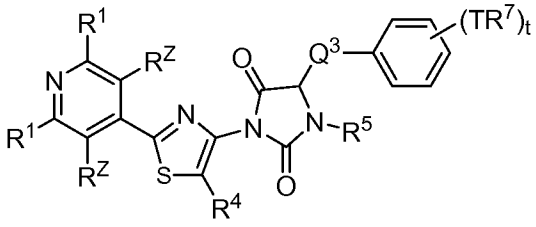


XXXI-A

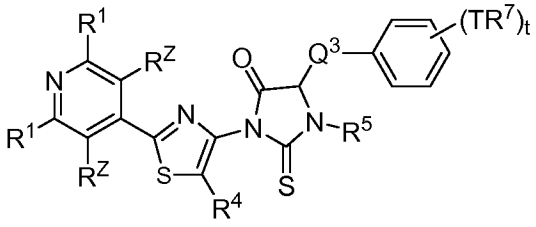




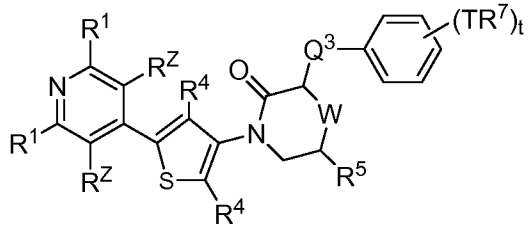
XXXII-A



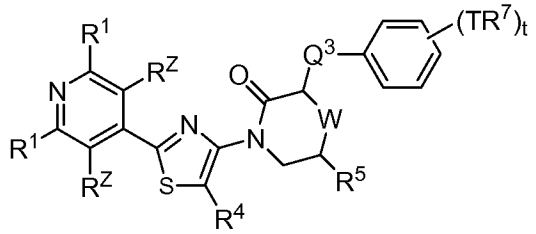
XXXIII-A



XXXIV-A



XXXV-A



XXXVI-A

XXXVII-A.

44. The compound of claim 43, wherein compound variables are selected from:

each occurrence of R^1 is hydrogen;

each occurrence of R^Z is hydrogen;

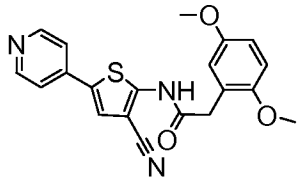
each occurrence of R^4 is independently hydrogen, $C_{1\text{-}6}$aliphatic, CN, $CON(R)_2$, or halogen;

R^5 is hydrogen, $(CH_2)_3OR'$, $(CH_2)_2OR'$, $(CH_2)OR'$, $(CH_2)_3N(R')_2$, $(CH_2)_2N(R')_2$, $(CH_2)N(R')_2$, or $C_{1\text{-}4}$aliphatic;

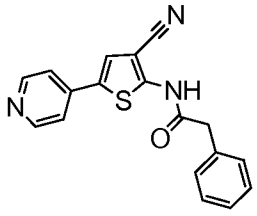
Q^3 is a direct bond, or is -$(CHR^6)_q$-, -$(CHR^6)_q$O-, -$(CHR^6)_q$S-, -$(CHR^6)_q$S(O)$_2$-, -$(CHR^6)_q$S(O)- , -$(CHR^6)_q$NR-, or –$(CHR^6)_q$C(O)-, wherein q is 0, 1, 2, or 3; and

t is 0, 1, 2, or 3, and each occurrence of TR^7 is independently -C_{1-3}alkyl, -OR′, -SR′, -CF_3, -OCF_3, -SCF_3, -F, -Cl, I, -Br, -COOR′, -COR′, -O$(CH_2)_4$N(R)(R′), -O$(CH_2)_3$N(R)(R′), -O$(CH_2)_2$N(R)(R′), -O(CH_2)N(R)(R′), -O$(CH_2)_4$CON(R)(R′), -O$(CH_2)_3$CON(R)(R′), -O$(CH_2)_2$CON(R)(R′), -O(CH_2)CON(R)(R′), -C(O)N(R)(R′), -$(CH_2)_4$OR′, -$(CH_2)_3$OR′, -$(CH_2)_2$OR′, -CH_2OR′, optionally substituted phenyl or benzyl, -N(R)(R′), -$(CH_2)_4$N(R)(R′), -$(CH_2)_3$N(R)(R′), -$(CH_2)_2$N(R)(R′), -(CH_2)N(R)(R′), -SO_2N(R)(R′), -NRSO_2R′, -CON(R)(R′), or -OSO_2R′.

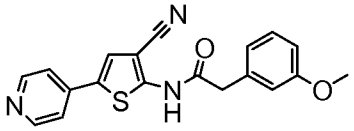
45. The compound of claim 1, having one of the structures:



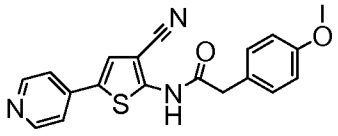
I-A-1



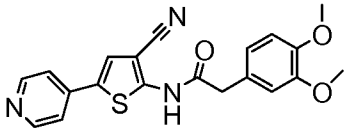
I-A-2



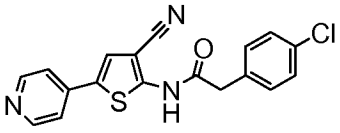
I-A-3



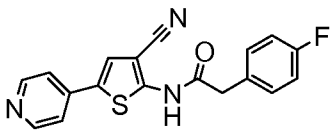
I-A-4



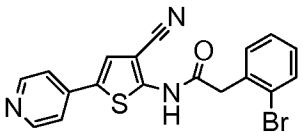
I-A-5



I-A-6



I-A-7



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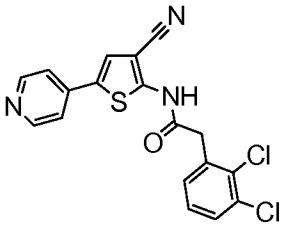

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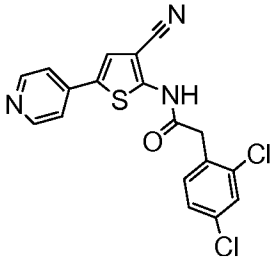
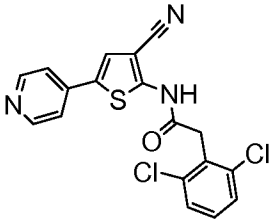


I-A-10



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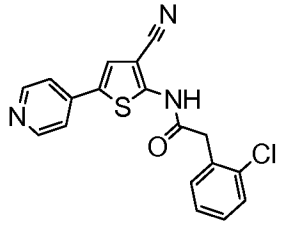

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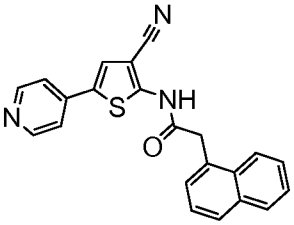

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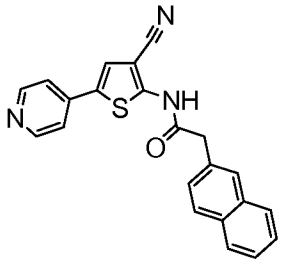

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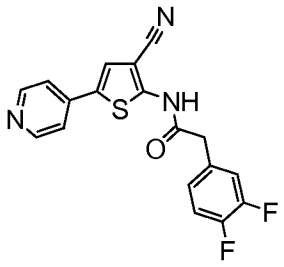

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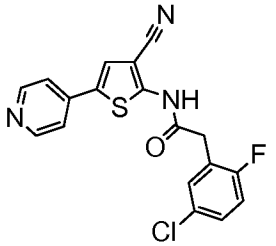
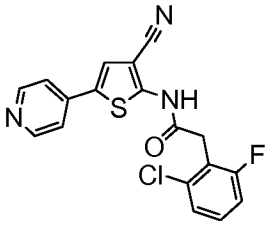


I-A-16



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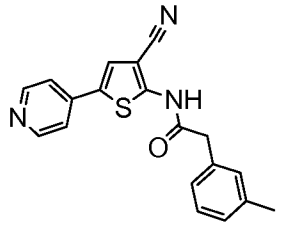
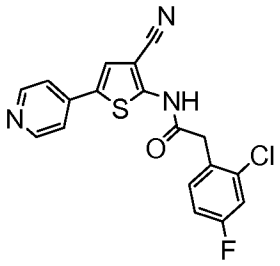
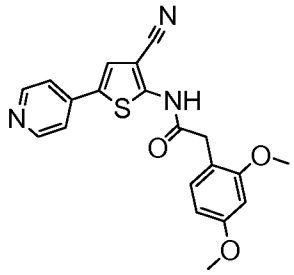


I-A-18



I-A-19



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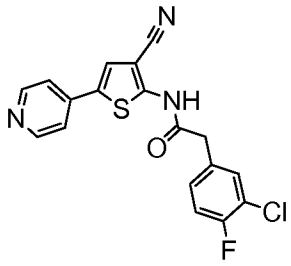

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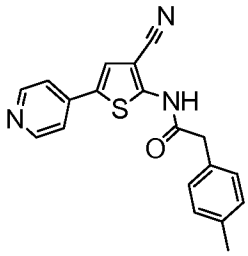

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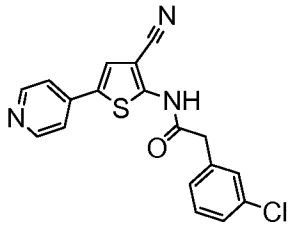
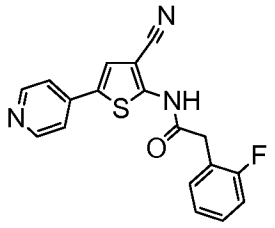
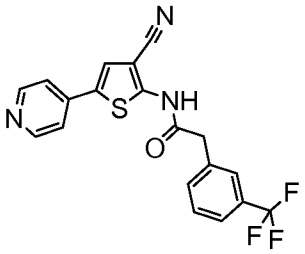


I-A-23



I-A-24



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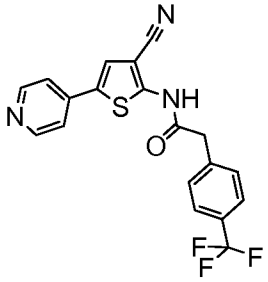

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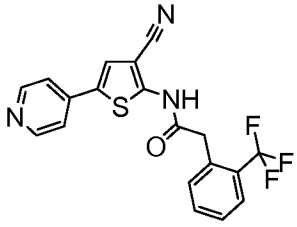

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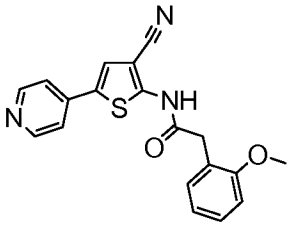
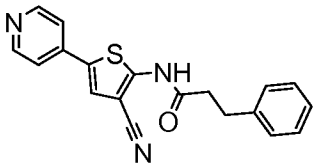


I-A-28



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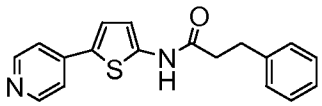

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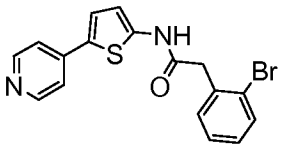

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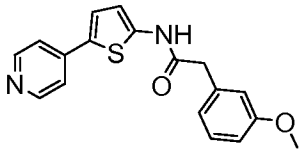

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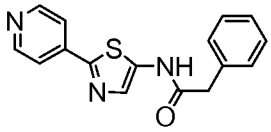

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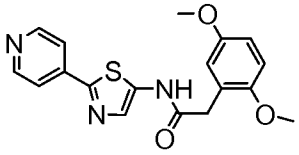

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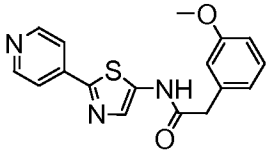

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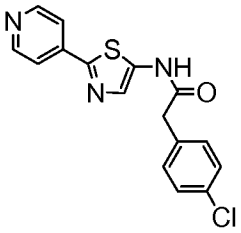

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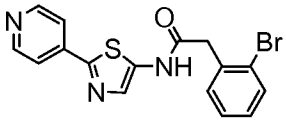

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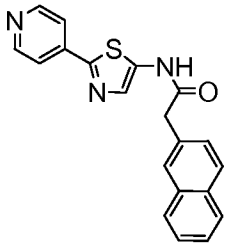

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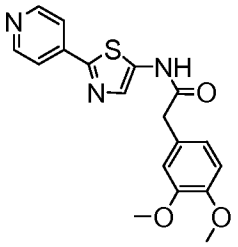

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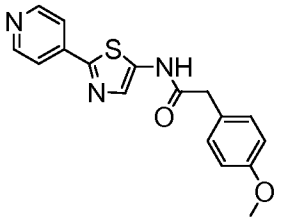

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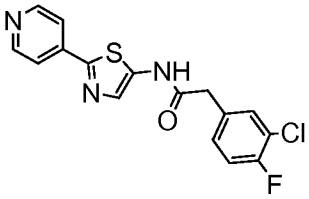

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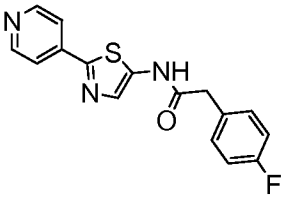

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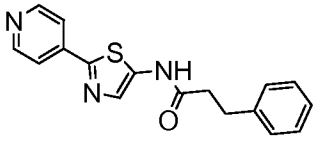

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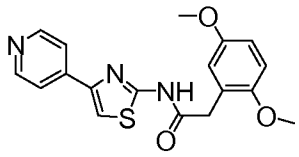

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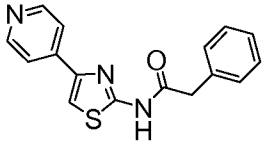

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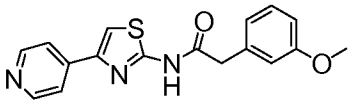

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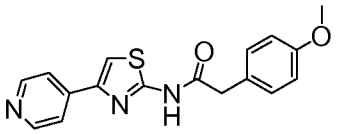

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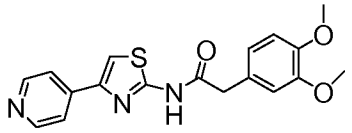

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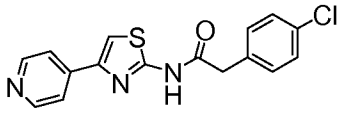

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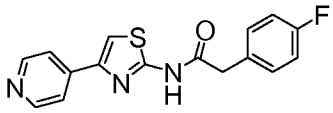

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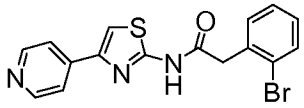

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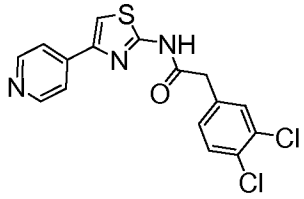

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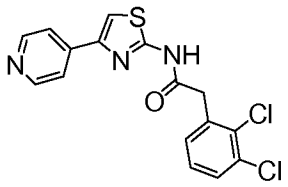

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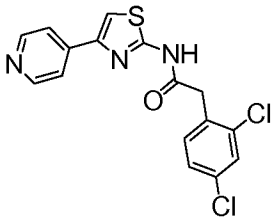

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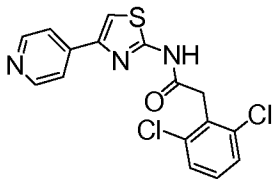

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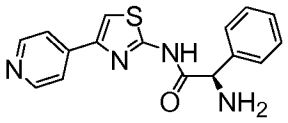

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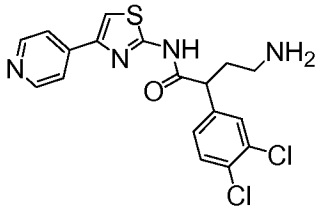

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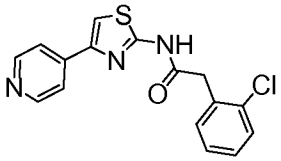

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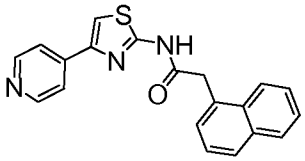

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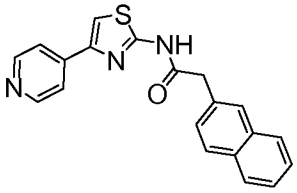

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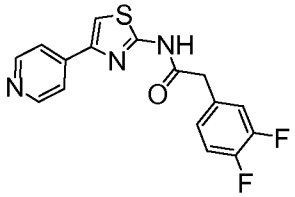

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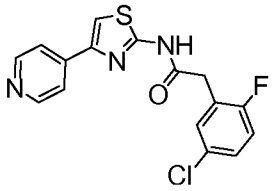

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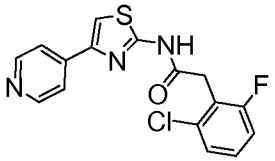

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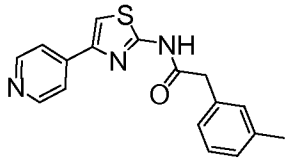

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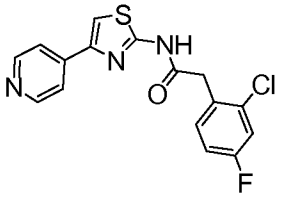

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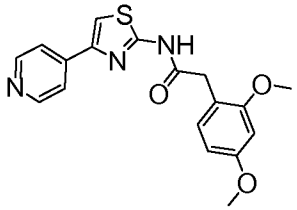

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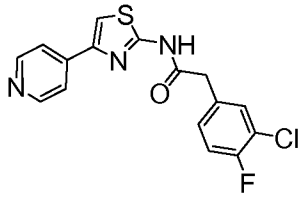

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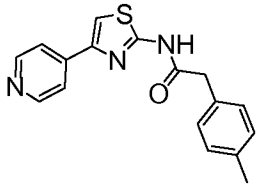

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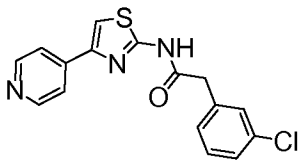

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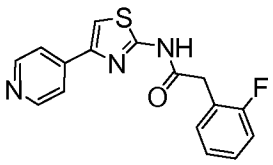

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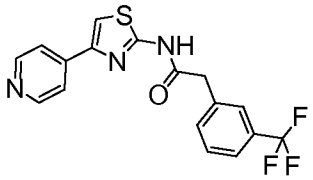
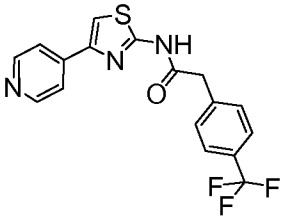
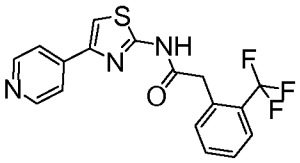


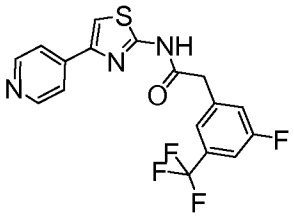
I-B-45



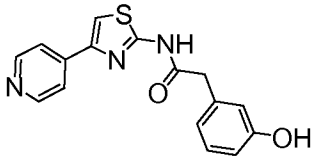
I-B-46



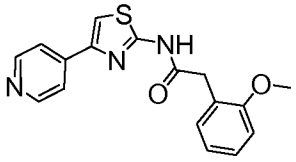
I-B-47



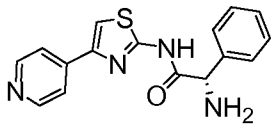
I-B-48



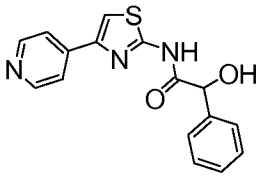
I-B-49



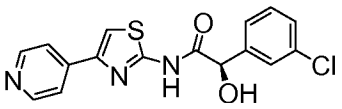
I-B-50



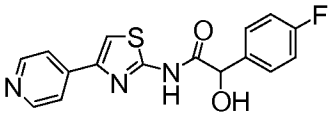
I-B-51



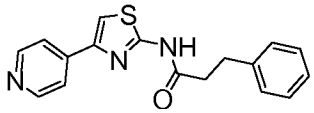
I-B-52



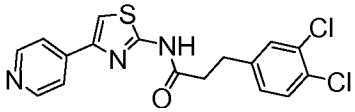
I-B-53



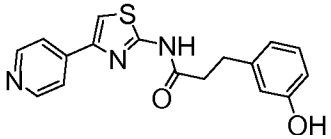
I-B-54



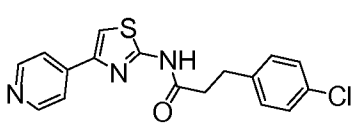
I-B-55



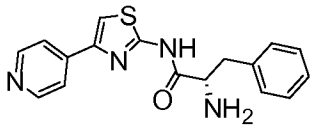
I-B-56



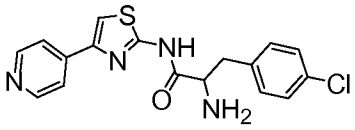
I-B-57



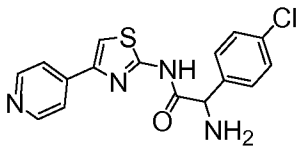
I-B-58



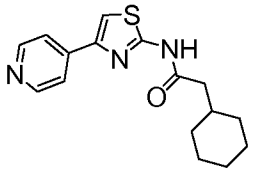
I-B-59



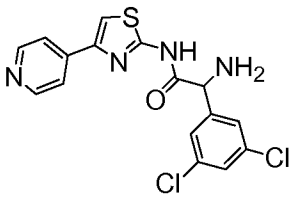
I-B-60



I-B-61



I-B-62



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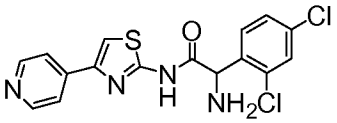

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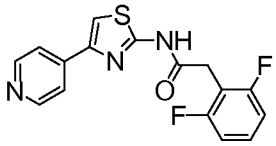

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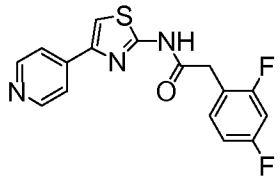
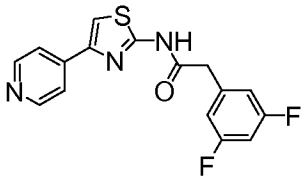
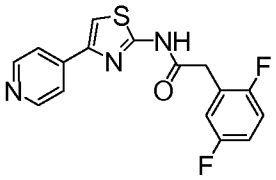


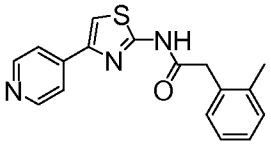
I-B-66



I-B-67



I-B-68



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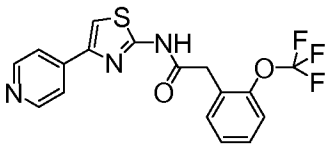
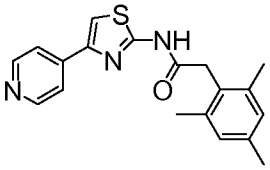


I-B-70



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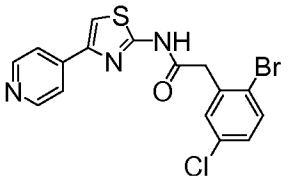
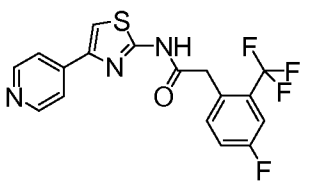
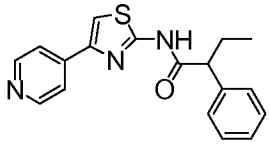


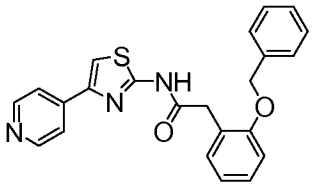
I-B-72



I-B-73



I-B-74



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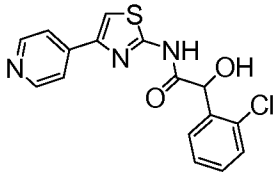

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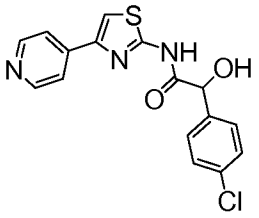

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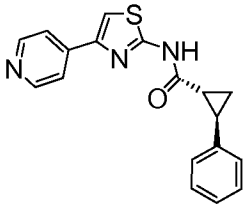

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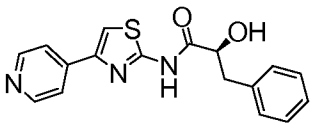

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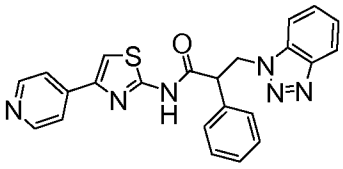

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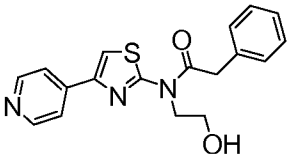

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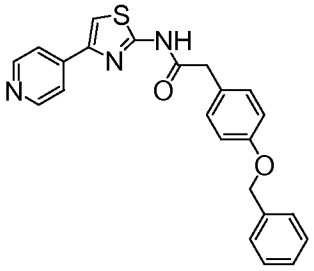

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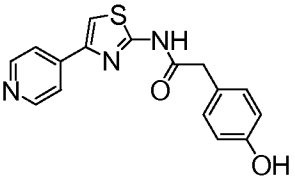

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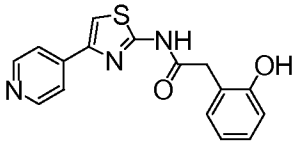

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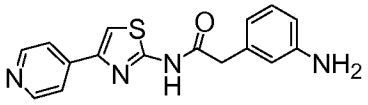

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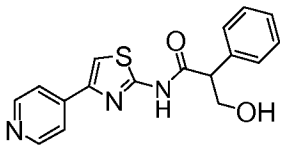

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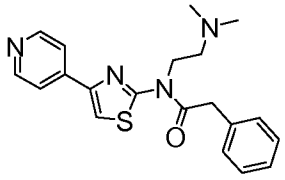

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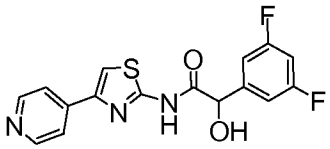

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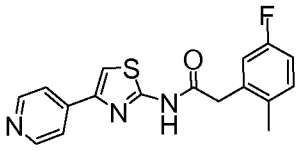

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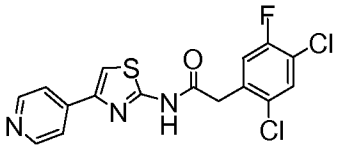

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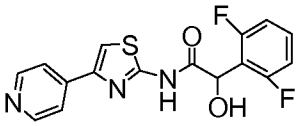

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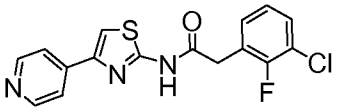

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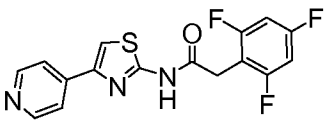

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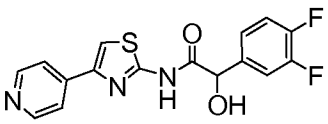

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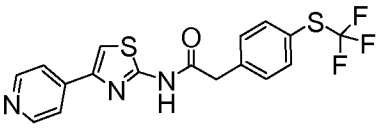

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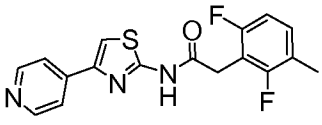

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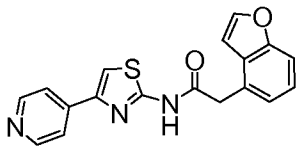
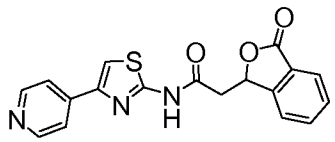
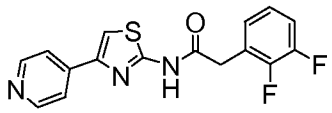


I-B-99



I-B-100



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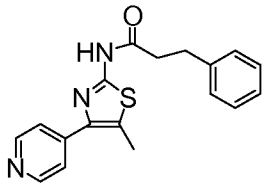

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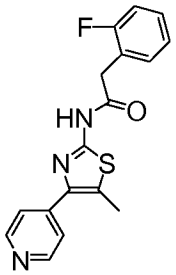

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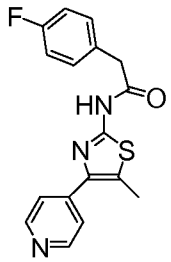

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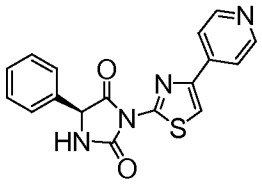

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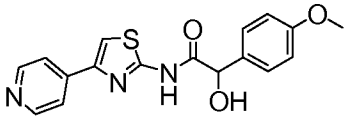
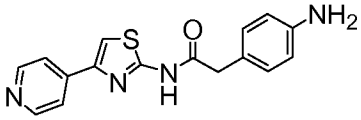
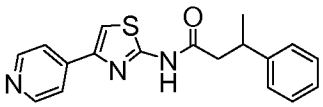


I-B-107



I-B-108



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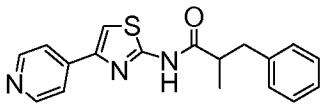

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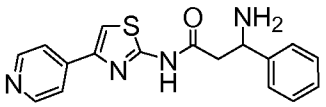
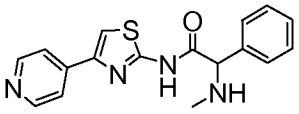
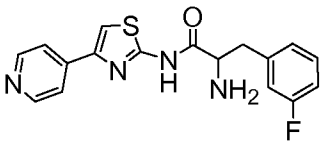


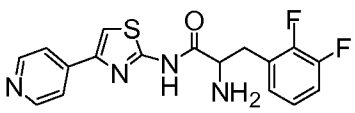
I-B-111



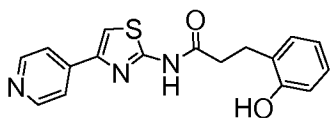
I-B-112



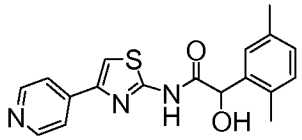
I-B-113



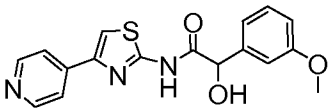
I-B-114



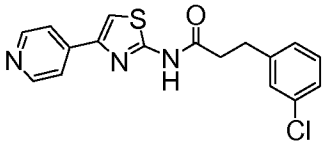
I-B-115



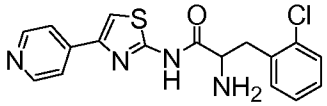
I-B-116



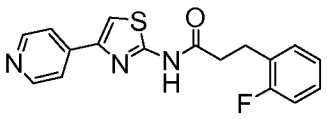
I-B-117



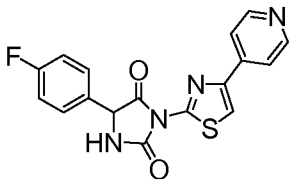
I-B-119



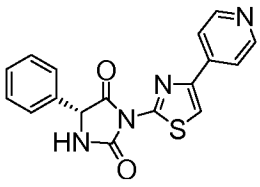
I-B-120



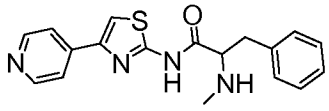
I-B-121



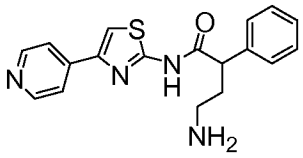
I-B-122



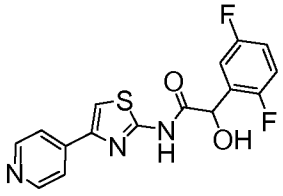
I-B-123



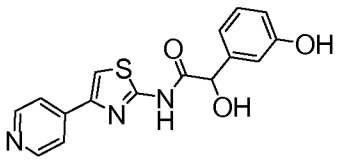
I-B-124



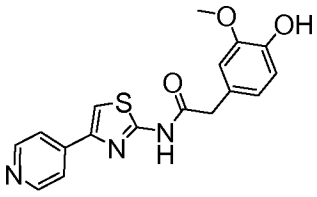
I-B-125



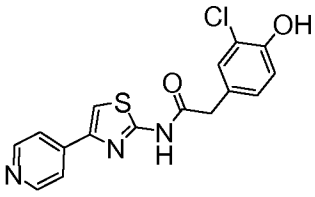
I-B-126



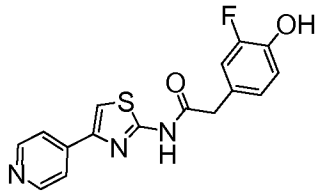
I-B-127



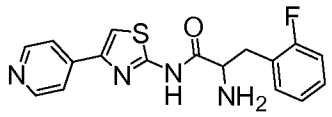
I-B-128



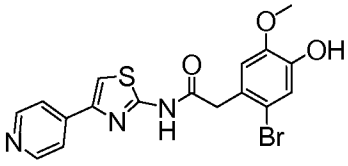
I-B-129



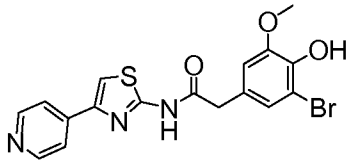
I-B-130



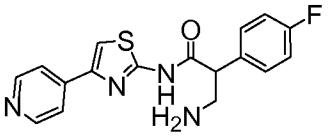
I-B-146



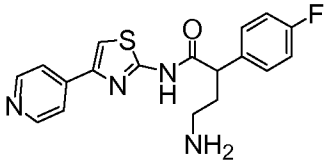
I-B-148



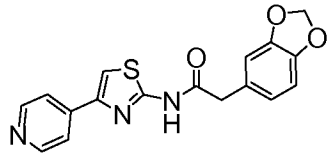
I-B-149



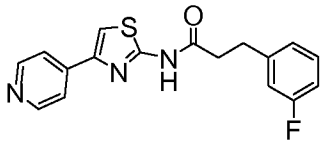
I-B-150



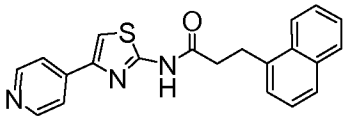
I-B-151



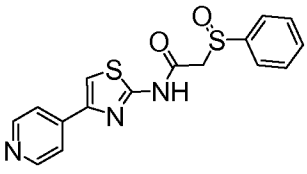
I-B-152



I-B-153



I-B-154



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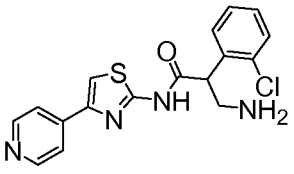
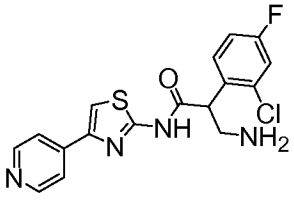


I-B-158



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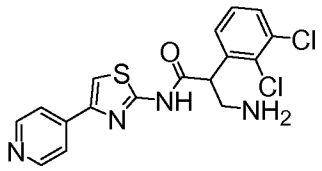
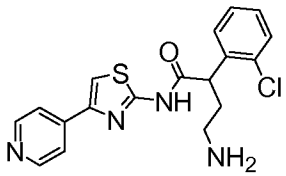
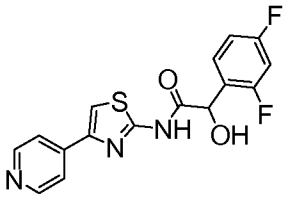


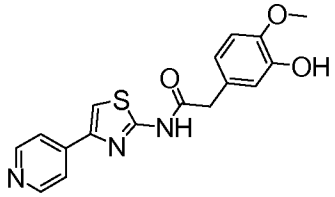
I-B-160



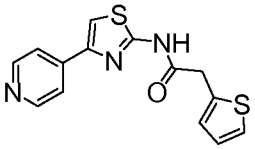
I-B-161



I-B-162



I-B-163



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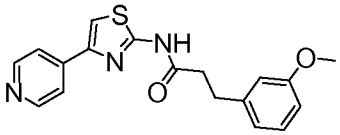
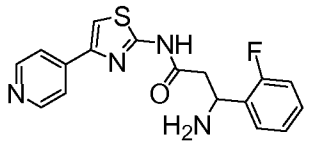
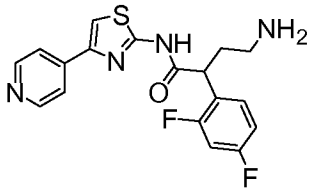


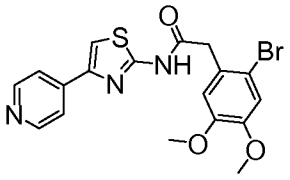
I-B-165



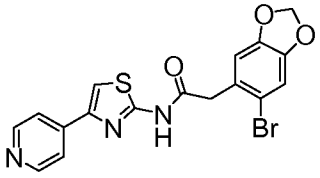
I-B-171



I-B-175



I-B-176



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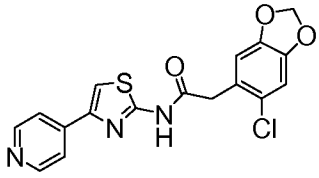
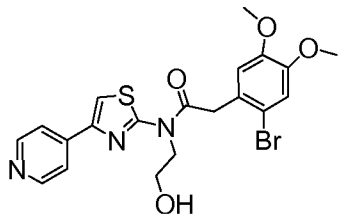
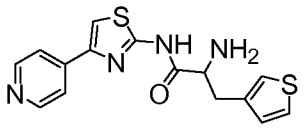


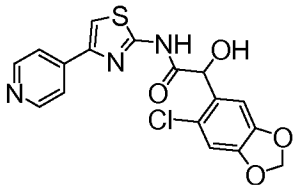
I-B-180



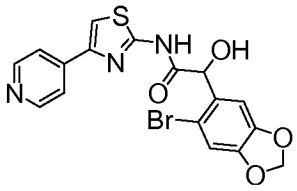
I-B-181



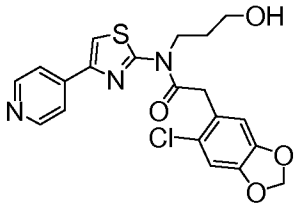
I-B-182



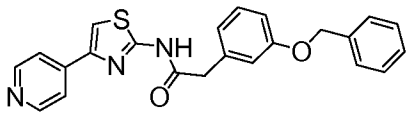
I-B-185



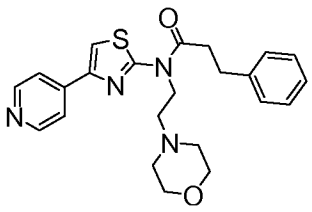
I-B-186



I-B-187



I-B-190



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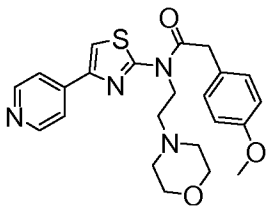

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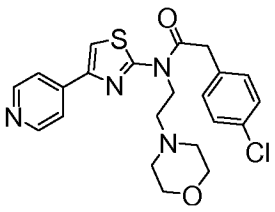

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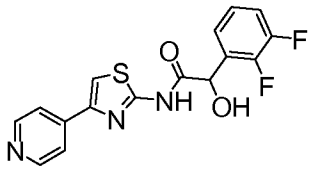
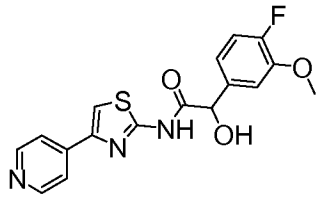
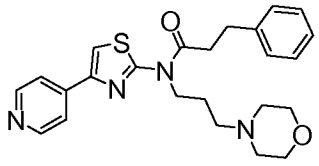


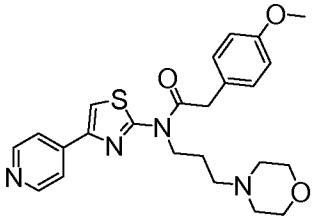
I-B-197



I-B-198



I-B-199



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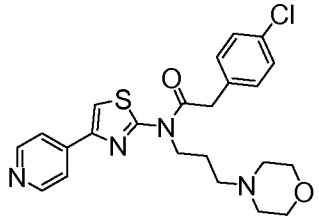
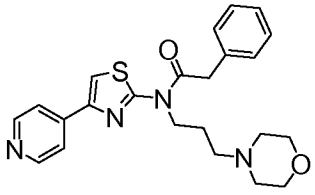
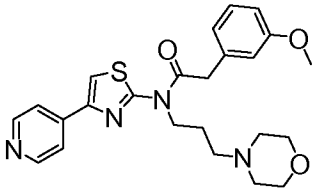


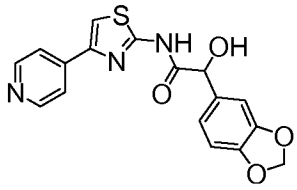
I-B-201



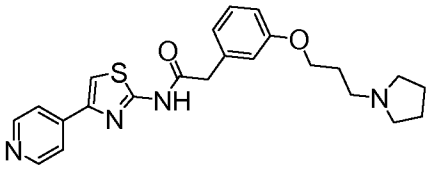
I-B-202



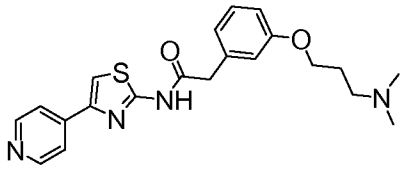
I-B-203



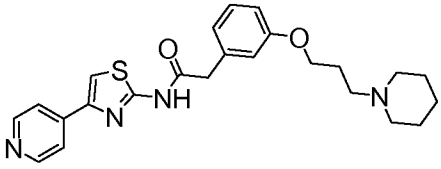
I-B-204



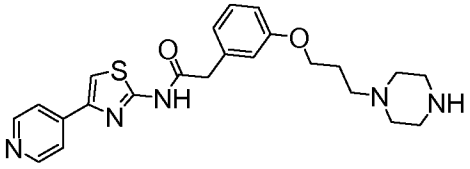
I-B-205



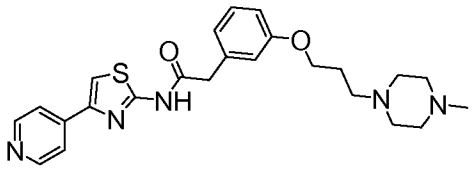
I-B-206



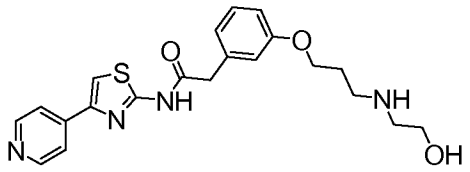
I-B-207



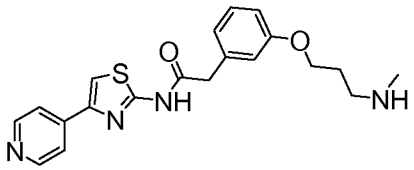
I-B-208



I-B-209



I-B-210



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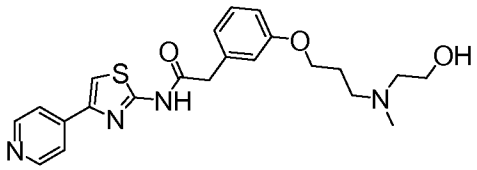
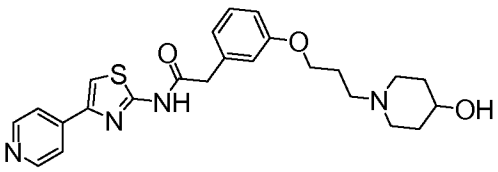


I-B-212



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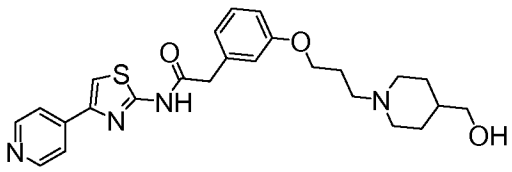

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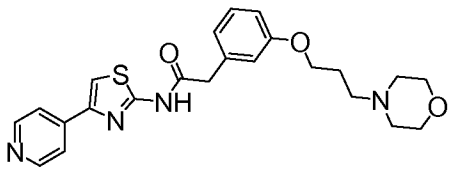

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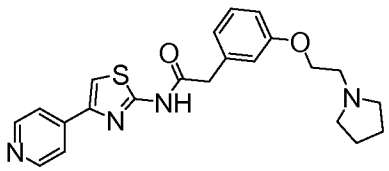

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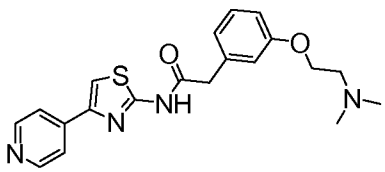

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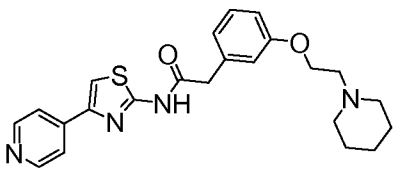

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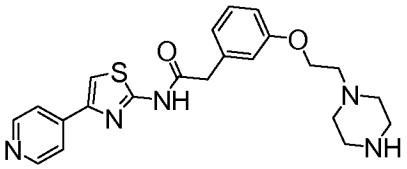

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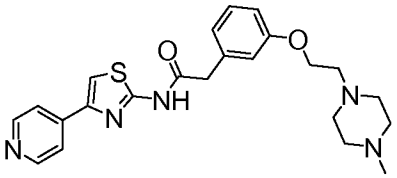

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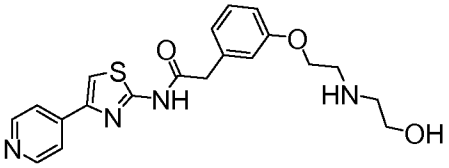

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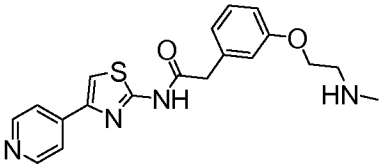

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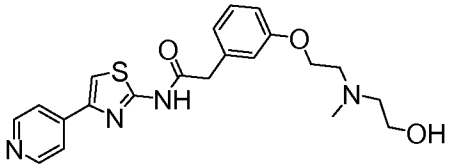

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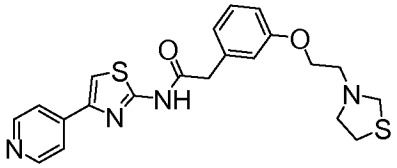

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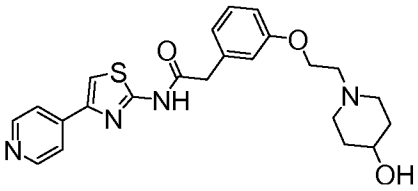

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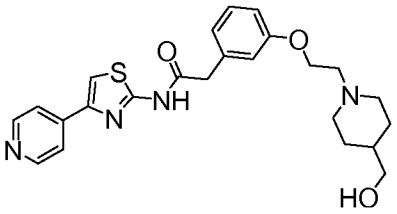

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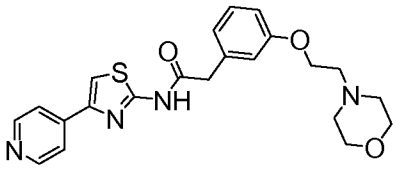

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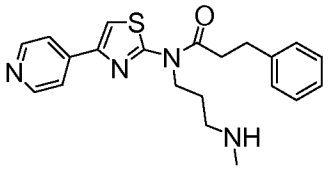

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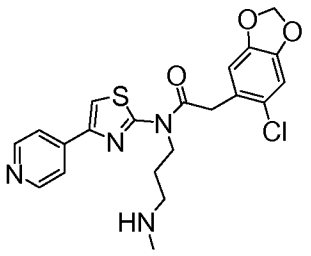

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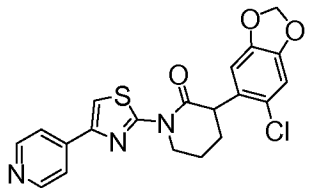

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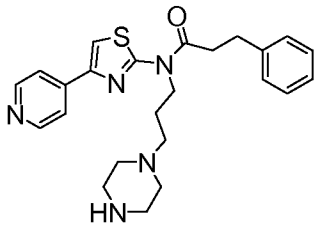

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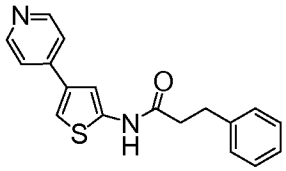

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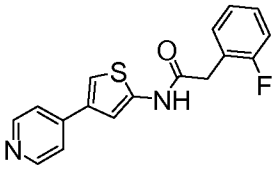

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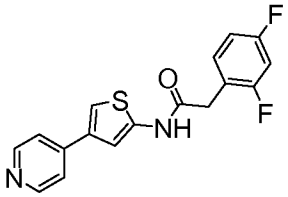

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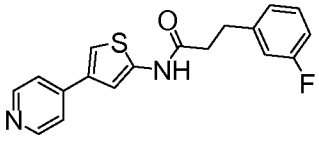

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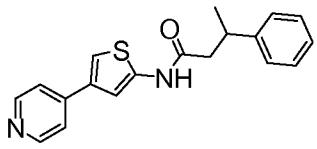

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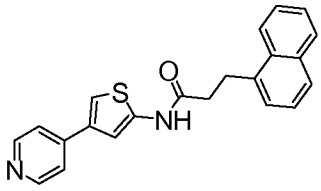

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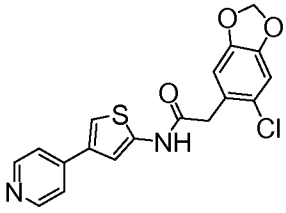

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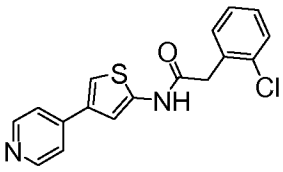

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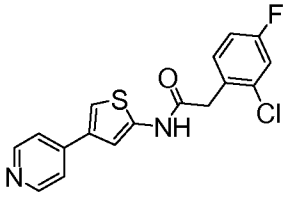

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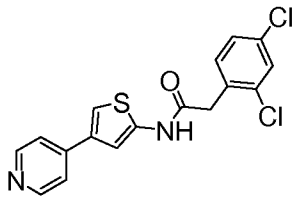

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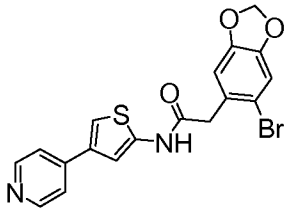

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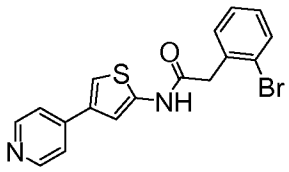

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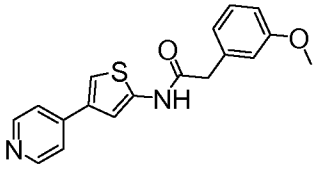

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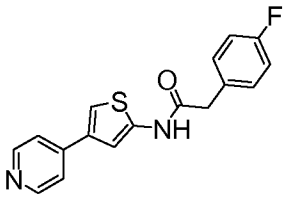

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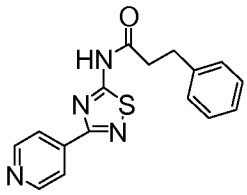

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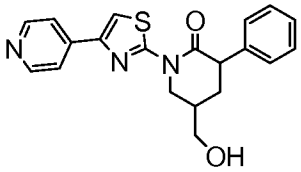

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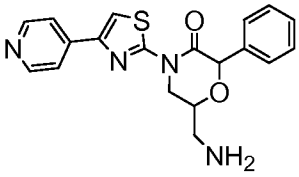

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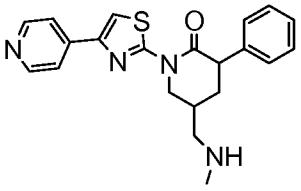

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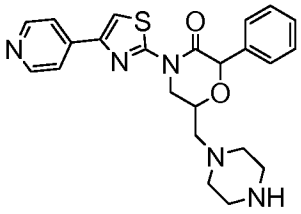

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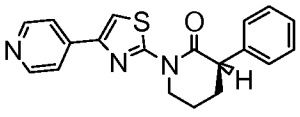

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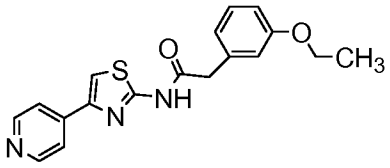

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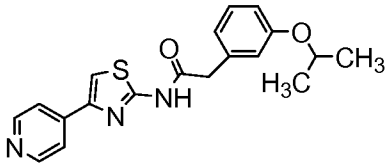

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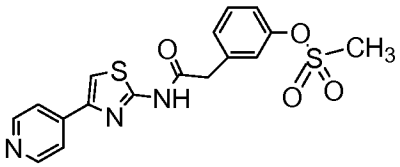

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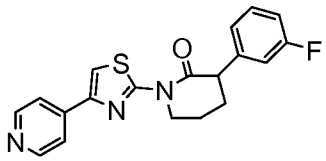
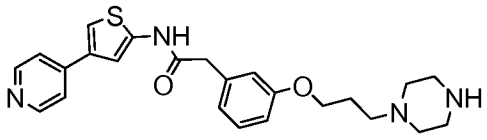
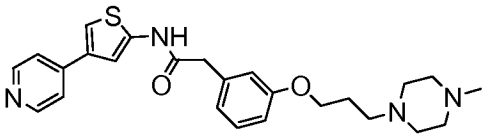


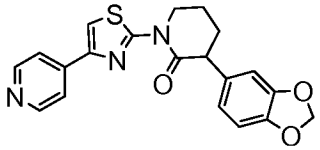
I-B-283



I-B-284



I-B-285



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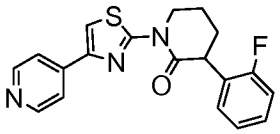
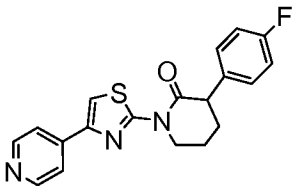


I-B-287



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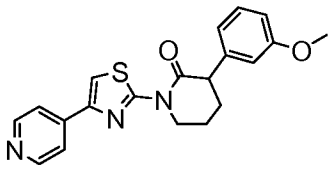

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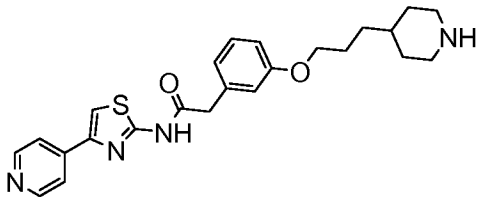

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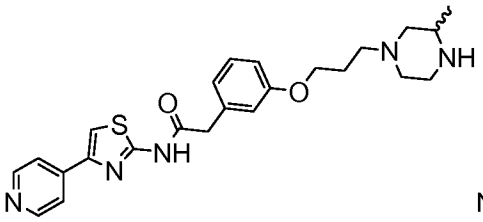

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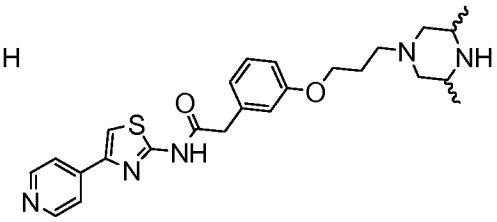

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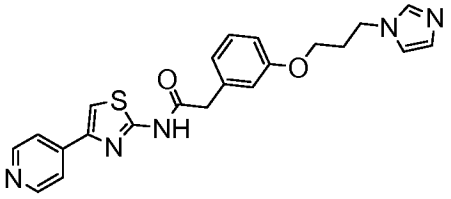
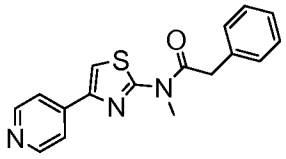
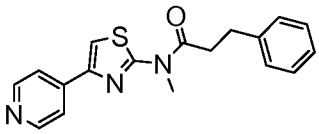


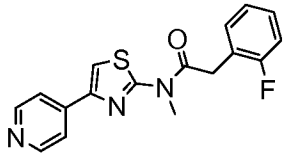
I-B-293



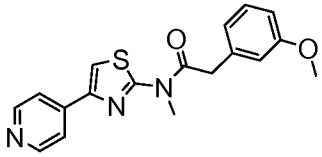
I-B-294



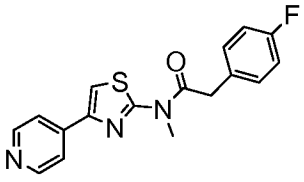
I-B-295



I-B-296



I-B-297



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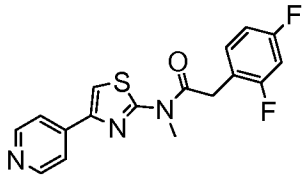
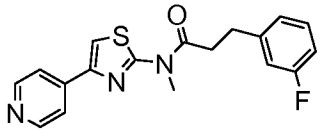


I-B-299



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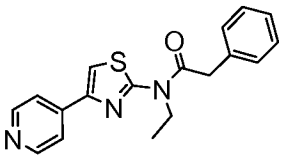
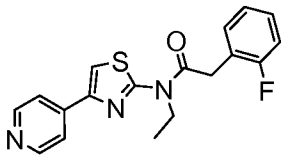


I-B-301



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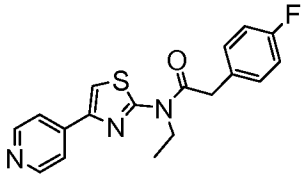
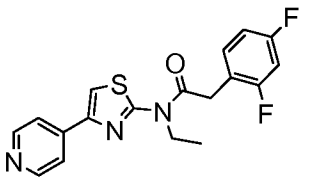
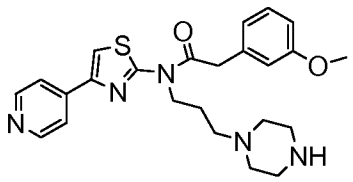


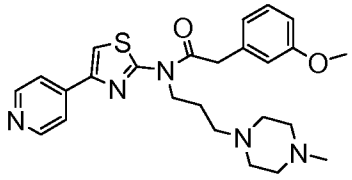
I-B-303



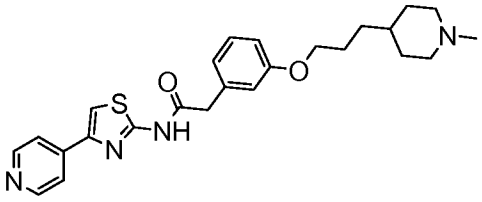
I-B-304



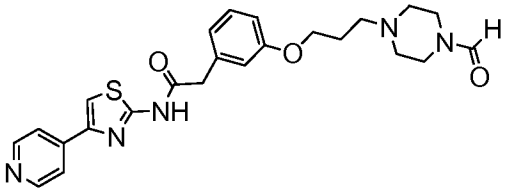
I-B-306



I-B-307



I-B-308



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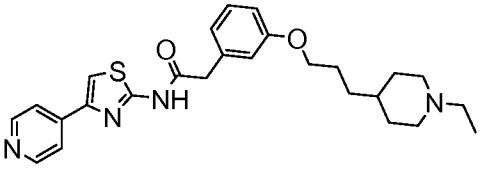
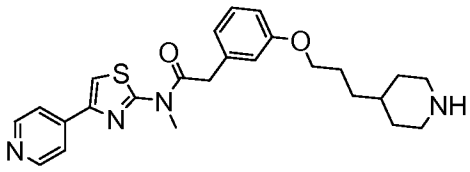


I-B-312



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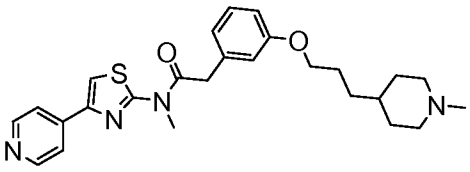

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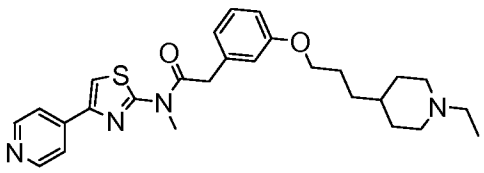

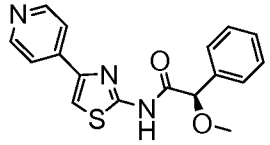

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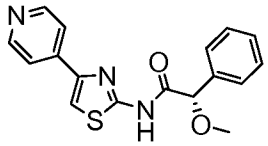
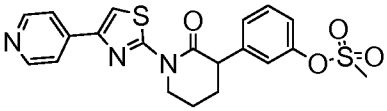
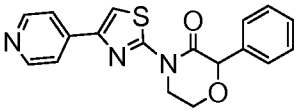


I-B-321





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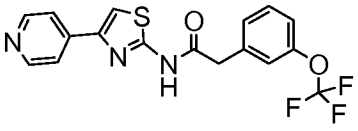
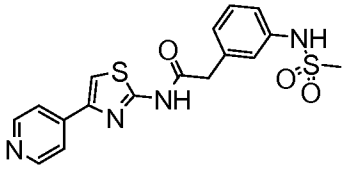


I-B-323



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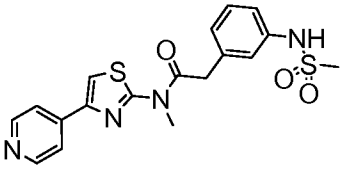
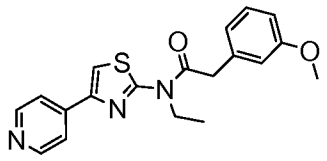


I-B-325

I-B-326

I-B-327

I-B-328



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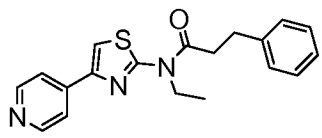

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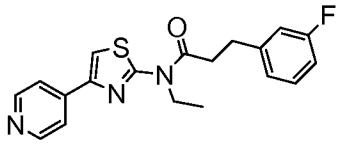

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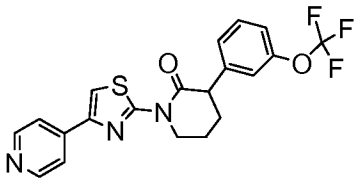

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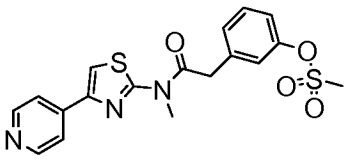

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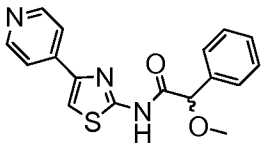
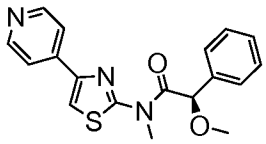
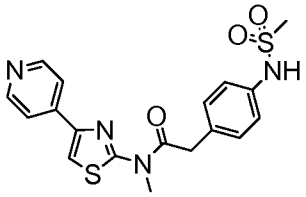
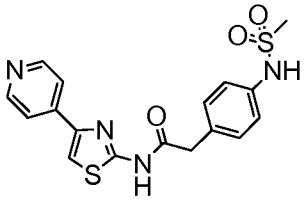
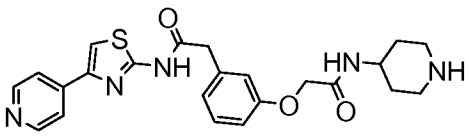




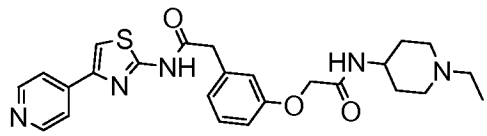




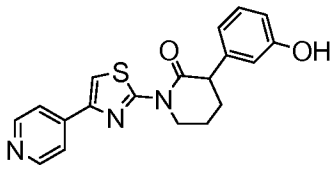
I-B-334



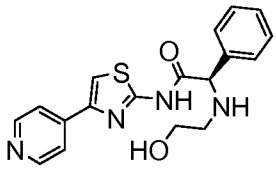
I-B-335



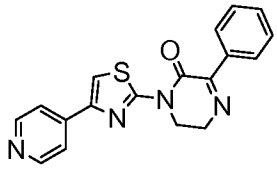
I-B-336



I-B-337



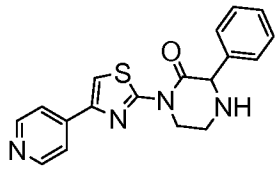
I-B-338



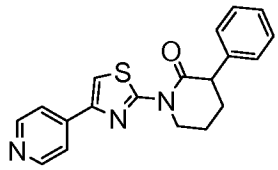
I-B-339

I-B-340

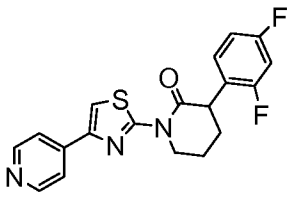
I-B-341



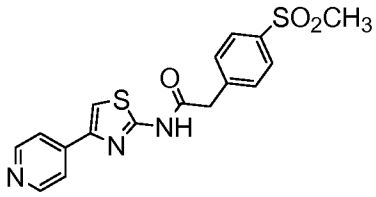
I-B-342



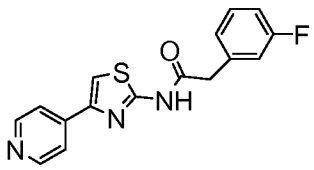
I-B-343



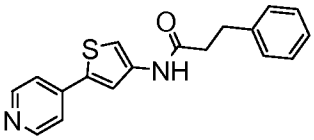
I-B-344



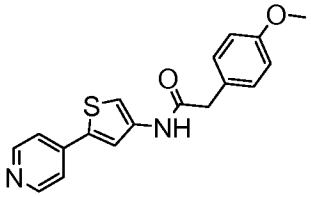
I-B-345



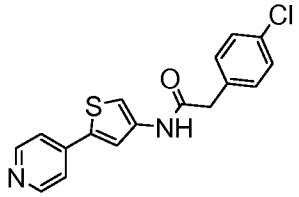
I-B-346



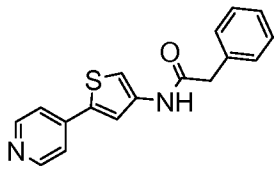
I-C-1



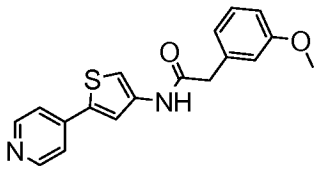
I-C-2



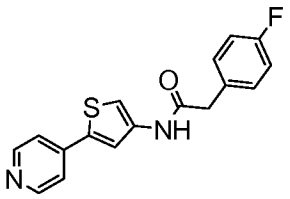
I-C-3



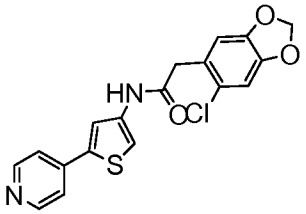
I-C-4



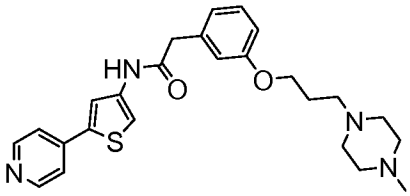
I-C-5



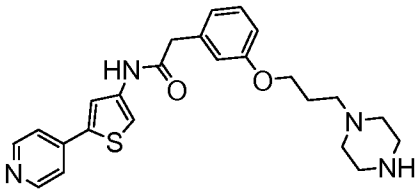
I-C-6



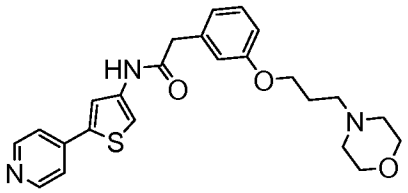
I-C-7



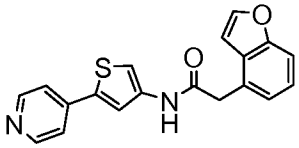
I-C-8



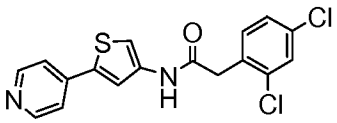
I-C-9



I-C-10



I-C-11



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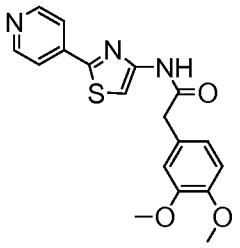

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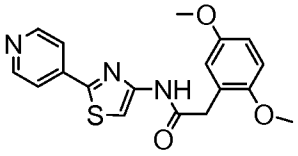

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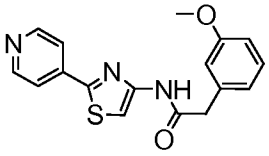

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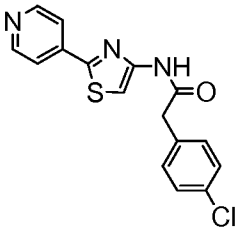

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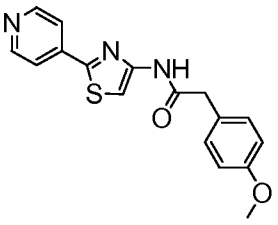

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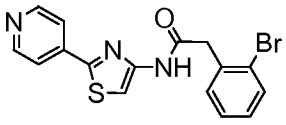

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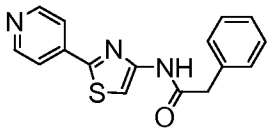

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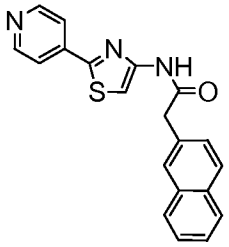

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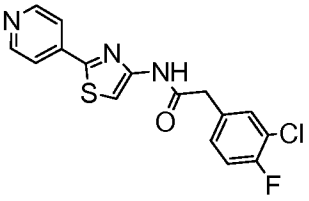

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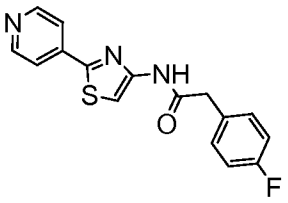

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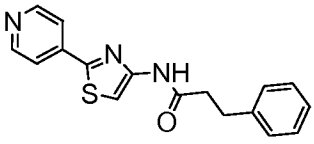

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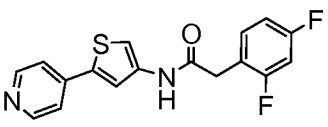

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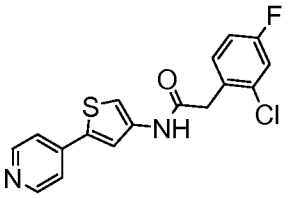

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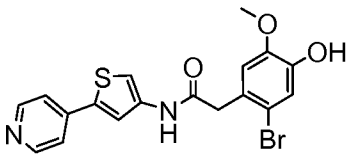

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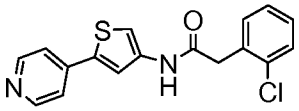
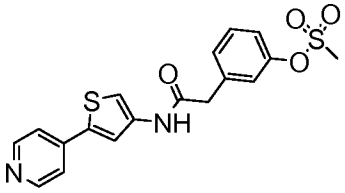


I-C-27



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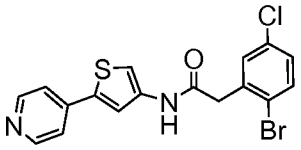

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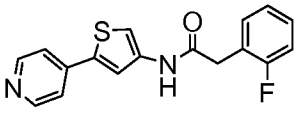

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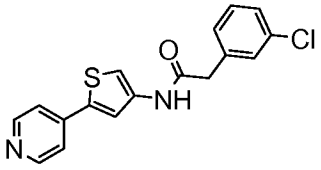

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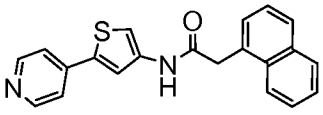
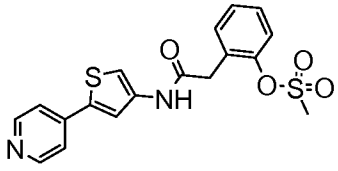
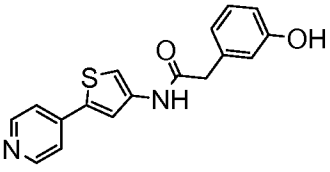


I-C-34



I-C-36



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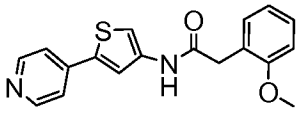

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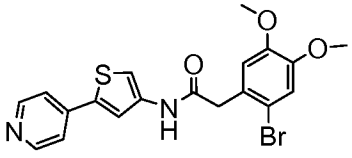

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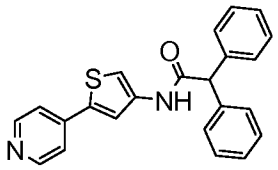


or **I-C-41**.

46. A composition comprising an effective amount of compound of claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

47-53. (Canceled)

54. A method of treating or lessening the severity of a disease or disorder selected from glaucoma, Alzheimer's disease, an allergy, asthma, or diabetes in a patient, said method comprising administering to said patient a compound according to claim 1.

55. The method of claim 54, wherein said method is used to treat or lessen the severity of an allergy or asthma.

56. The method of claim 54, wherein said method is used to treat or lessen the severity of diabetes.

57. The method of claim 54, wherein said method is used to treat or lessen the severity of glaucoma.

EVIDENCE
(Japanese Patent Application No.: 2002053566

1.This document has been translated by computer. So the translation may not reflect the original precisely.
2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention]This invention relates to the salt permitted on a new thiazole compound or medicine manufacture, and the medicinal composition which contains them as an active principle. [check / selectively / especially / checking proteinkinase C (PKC) activity in detail and / PKC isozyme gamma (PKCgamma) activity] It is related with the salt permitted on the new thiazole compound which has an analgesic action, or medicine manufacture, and the medicinal composition which contains them as an active principle.
[0002]
[Description of the Prior Art]PKC is a kind of serine / threonine protein kinase which plays a central role in intracellular various signal transduction. The protein which PKC phosphorylates An epidermal growth factor receptor, an insulin receptor, Receptors, such as an interleukin 2 receptor, an acetylcholine receptor, and adrenoreceptor, A large number, such as metabolic enzymes, such as glycogen phosphorylase kinases, such as much membrane protein, such as phospholamban, a sodium ion channel, and a glucose carrier, actin which constitutes muscles, and myosin, and a cytochrome P-450, are covered. It is known that at least ten or more sorts of isozymes exist in PKC now. These isozymes take the structure which allotted the kinase domain to the C terminal side and they matched for the amino terminal side with the control domain. [each] Between PKC(s), a kinase domain shows high homology and indicates homology to be other protein kinases, such as A kinase (it is also called cyclic AMP dependent protein kinase and PKA.), G kinase (cyclic GMP dependent protein kinase), and tyrosine kinase. All over a control domain, a calcium binding site and a phorbol ester binding site exist, and it can distinguish to a group {alpha, beta (an I-beam, II type), gamma} which has the both, a group (delta, epsilon, theta, eta) which has only a phorbol ester binding site, and a group (zeta, lambda) lacking in the both. Are activated with the metabolite and calcium of cell

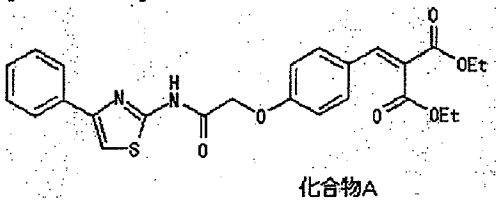
membrane inositol phospholipid, such as diacylglycerol (DAG), namely, PKCalpha, beta, and gamma are phospholipid / calcium dependent serine / threonine protein kinase.
[0003]As condition of disease through PKC activation, the fall of a contraction response and the increase in production of an extracellular matrix are mentioned in vasoconstrictor abnormalities, such as abnormalities in a blood flow, such as a retina blood-flow fall, blood-vessel-permeability sthenia of the vasa sanguinea retinae, and sthenia of a mesangium filtration value, and a kidney mesangial cell. There are various reports, such as being involved in symptoms, such as cardiac hypertrophy and heart fibrillation, in the abnormalities in cell growth by activation of a transcription factor and the abnormalities in gene expression, and the cardiac muscle tissue. therefore, the drugs which check PKC activity -- diabetic complications (diabetic retinopathy.) Adaptation for various diseases, such as diabetic nephropathy, diabetic cardiomyopathy, a diabetic neuropathy, arteriosclerosis, an angiopathy, inflammation (thrombosis etc.), a dermatosis, immune diseases (acquired immunodeficiency etc.), central nervous system diseases (Alzheimer disease etc.), and cancer, can be considered.
[0004]A report of painkilling is also seen as a pharmacological action of PKC inhibitor. It was known that it will be mostly revealed to a central nervous system, and since PKC existed especially in a posterior horn of spinal cord mostly, it was expected to show a certain influence in a pain. It was reported that PDBu (phorbor 12 13-dibutyrate) of PKCbeta inhibitor controls inflammatory pain irritation (Neurosci.Lett., 140,181-184-1992), and the operation about the pain of PKC inhibitor was proved in 1992. Also in the PKC isozyme, as for PKCgamma, the manifestation is observed only in the brain and the spine, and adaptation in tolerance [as opposed to narcotic analgesics, such as a pain a hyperalgesia, allodynia and morphine, in especially a PKCgamma selective inhibition agent] is expected. In the laboratory animal from which morphine tolerance was acquired by the repetitive administration of morphine in 1995, it is reported that the immune activity of PKCgamma increased clearly by the posterior horn of spinal cord (BRAIN RESEARCH and 677 (2).) As a result of prescribing 257-67-1995, morphine, and PKC inhibitor for the patient collectively, having prevented morphine tolerance was also reported (PAIN, 85 (3), 395-404-2000). Although oversensitive condition and a continuous pain may be caused by the injury of a peripheral nerve in an ordinary animal, In the laboratory animal made to lack PKCgamma, not having almost developed in the shape of nervous pain thoroughly is reported, and the possibility to prevention and the therapy of a continuous pain is shown (SCIENCE, 278 (5336), 279-83-1997). The opinion it is supposed that PKCgamma has contributed to continuation of the allodynia caused by peripheral inflammation is proposed in 1999 (NEUROSCIENCE, 88 (4), 1267-74-1999). Many compounds which have PKC inhibitory action are already reported. among these -- comparing some inhibitor with other kinase -- PKC -- alternative selectivity [in / nevertheless / an isozyme] is insufficient -- etc. -- it has not resulted in development of still practical drugs for the

reason. If PKC takes into consideration playing a central role in intracellularsignal transduction, In particular, in a cell and an organ with much distribution of PKCgamma, the condition which activates PKCgamma selectively, and the condition to which PKCgamma relates deeply, it is desirable to check PKCgamma activity selectively, and a PKCgamma selective inhibition agent is expected as safety and a development target of drugs with few side effects.

[0005]The chronic pain produced from damage, the functional disorder, etc. of the nerve after [which it mourned over and also injury recovered] being caused by a trauma, a surgical operation, inflammation, etc. is one of the big problems of clinical. The pain depended unusually [sensory nerves, such as a hyperalgesia which shows sthenia of a reaction to the painful usual stimulus, and allodynia which senses a pain to the stimulus which does not feel a pain when normal,] may also develop into a serious condition which interferes with a life. Now, morphine is begun and some analgesics are used. However, while narcotics nature and nonnarcotic opioid show a strong analgesic action, they show physical dependence and psychic dependence nature, and present the withdrawal. Since condition, such as a respiratory depressant effect, nausea, vomiting, constipation, and dysuria, appears as other side effects, it has a fault referred to as that the use is restricted. The condition which shows resistance to the analgesic usually used for the pain which happens by nervous damage, functional disorder, etc. by clinical now, for example, an antipyretic analgesic and a narcotic analgesic, and does not show an effective analgesic action is also seen. Therefore, development of the drugs which improve the tolerance of narcotic analgesics, such as a painkiller received unusually [sensory nerves, such as a powerful painkiller which does not have the painkiller, especially addiction which combine safety and validity a hyperalgesia, and allodynia,], and morphine, is desired.

[0006]Here, the prior art reference which indicates the thiazole compound of this invention and the compound with which structure is comparatively similar is introduced. The following compound A etc. are indicated as PKC inhibitor by JP,10-287634,A.

[Formula 7]



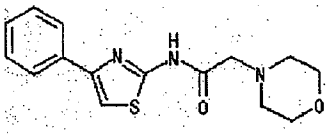
化合物A

However, the chemical structure features [the invention compound and this invention compound of this patent] differ, and suggestion of this invention compound is not seen, either.

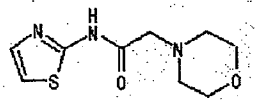
[0007]The anti-inflammation effect of the following compound B and the analogue is shown in Pharmazie, 48 (12), and 948-949 (1993).

The analgesic effect is also shown by the examination of anti-inflammation about the following compound C with the highest effect.

[Formula 8]



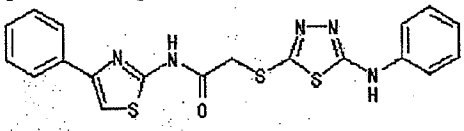
化合物B



化合物C

[0008]The following compound D is indicated by J.Indian Chem.Soci., 57 (12), and 1241-3 (1980) as acetylcholineaterase inhibitor.

[Formula 9]

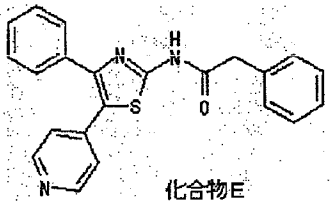


化合物D

The following compound E is indicated by WO 99/No. 21555 as an adenosine A3 receptor antagonist.

The use as a treating agent to the asthma of this compound, the allergosis, inflammation, etc. is described.

[Formula 10]

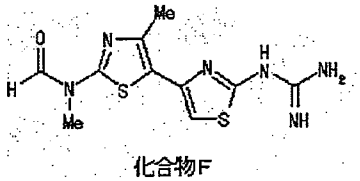


化合物E

[0009]The following compound F is indicated by JP,59-193878,A (US4649146, US4735957, EP117082).

The strong heart operation of this compound and the antiulcer action are described.

[Formula 11]



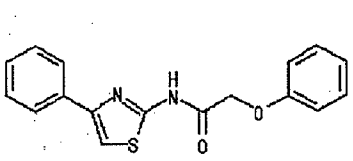
化合物F

However, although these articles have the statement about the medicine use of this

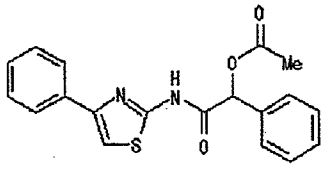
compound, there is no statement which teaches this invention compound, and the statement about PKC inhibiting activity is not seen, either.

[0010]On the other hand, following amide compound G is indicated by FR No. 2073282, and following amide compound H is indicated by Indian J.Chem., 1 (10), and 441-2 (1963).

[Formula 12]



化合物G



化合物H

However, the amide compound indicated by these literature stops at being indicated as an intermediate of the compound which only has an analgesic action.

[0011]

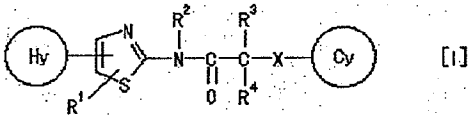
[Problem(s) to be Solved by the Invention]PKC inhibitor can turn into drugs which treat or/and prevent the various symptoms relevant to PKC by these knowledge. Without spoiling normal intracellularsignal transduction, especially a PKCgamma selective inhibition agent turns into safe drugs in which remarkable side effects are not shown, especially can turn into therapies (tolerance over narcotic analgesics, such as a pain, a hyperalgesia, allodynia, and morphine, etc.) over which it mourns, and preventive. Therefore, the purpose of this invention is to provide the drugs which have PKC inhibitory action, especially the drugs which have a PKCgamma selective inhibition operation.

[Means for Solving the Problem]

[0012]This invention persons came to complete this invention, as a result of repeating research wholeheartedly in order to find out a compound which has high PKC inhibitory action and has a PKCgamma selective inhibition operation. It is as being shown in following (1) thru/or (11) in more detail.

[0013](1) Proteinkinase C inhibitor containing the salt permitted on a thiazole compound expressed with following general formula [I], or medicine manufacture.

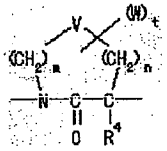
[Formula 13]



[I]

R^1 among [type A hydrogen atom, a halogen atom, Are a C_{1-6} alkyl group and R^2 Or a hydrogen atom, Or it is a C_{1-6} alkyl group which may be replaced by the substituent chosen from the following group A, and they are a {group A:halogen atom and $-OR^{b1}$ (R^{b1} among a

formula). they are a hydrogen atom or a C_{1-6} alkyl group $-SR^{b2}$ (the inside of a formula, and R^{b2} -- a hydrogen atom.) or it is a C_{1-6} alkyl group -- and $-NR^{b3}R^{b4}$ (R^{b3} and R^{b4} among a formula) same respectively or differing -- a hydrogen atom and a C_{1-6} alkyl group. Or the heterocycle group which is a heterocycle group which becomes together with the nitrogen atom in which R^{b3} and R^{b4} adjoin, and is formed, becomes together with the nitrogen atom which this adjoins here, and is formed, Besides one nitrogen atom, it may be replaced by a C_{1-6} alkyl group including 0 thru/or 3 hetero atoms chosen from an oxygen atom, a nitrogen atom, or a sulfur atom. . }R^3 and R^4 are the same respectively, or differ from each other, The C_{1-6} alkyl group, $-OR^{a1}$ (R^{a1} among a formula) which may be replaced by the substituent chosen from a hydrogen atom and the above-mentioned group A they are a hydrogen atom, a C_{1-6} alkyl group, or a C_{1-6} alkyl carbonyl group. Or the inside of a $-NR^{a2}R^{a3}${type, R^{a2}, and R^{a3}, It is a heterocycle group (passage of said definition.) which becomes together with the nitrogen atom in which it differs and a hydrogen atom, a C_{1-6} alkyl group, a C_{1-6} alkoxycarbonyl group or R^{a2}, and R^{a3} adjoin respectively identically, and is formed. It is} and R^2 and R^3 become together with adjoining -N-CO-CR^4-, [Formula 14]

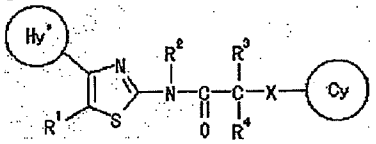


{V among a formula $-CH_2-$, -O-, -S-, -CO-, -OCO-, $-NR^{a5}-$, $-CO-NR^{a5}-$, Or $-NR^{a5}-CO$ - (here, R^{a5}) A hydrogen atom, C_{1-6} alkyl group, and C_{6-14} aryl C_{1-6} alkyl group, a C_{1-6} alkoxycarbonyl group, Or it is a C_{6-14} aryl C_{1-6} alkyloxy carbonyl group. W C_{1-6} alkyl group, or when it is a substituent chosen from the above-mentioned group A, t is 0, 1, or 2 and t is 2, two W is the same respectively -- or it may differ and m and n are the same respectively -- or it differs and is an integer of 0, or 1 thru/or 3. May form a ring expressed with} and X A single bond, C_{1-4} alkylene, -O-, -S-, -COO-, -OCO-, $-NR^{a4}-$, $-CO-NR^{a4}-$, Or it is $-NR^{a4}-CO-$ (R^{a4} is a C_{1-6} alkyl group which may be replaced by hydrogen atom or a substituent chosen from the above-mentioned group A among a formula.), [0014]The ring Hy is a heterocycle group and here this heterocycle group, Including 1 thru/or 4 hetero atoms chosen from an oxygen atom, a nitrogen atom, or a sulfur atom, this heterocycle group, when it may be replaced by 1 thru/or 3

substituents chosen from the following group B and this substituent is two pieces or three pieces, this substituent is the same respectively -- or the {group B:nitro group which may differ, a halogen atom, and -Y-Z[-- here, Y A single bond, -CH=CH-, -O-, -CH(OH)-, -COO-, - NR^{b5}-, - NR^{b6}-CO-, -NR^{b7}-COO-, - NR^{b8}-CO-NR^{b9}-, -NR^{b10}-SO_2-, and -CO-NR^{b11}- (the inside of a formula, and R --) [^{b5} and] R^{b6}, R^{b7}, R^{b8}, R^{b9}, R^{b10}, and R^{b11} A hydrogen atom, Or it is a C_{1-6} alkyl group. A C_{1-6} alkyl group by which Z may be replaced by a substituent as which it is chosen out of a hydrogen atom and the above-mentioned group A, a C_{6-14} aryl group, a C_{3-7} cycloalkyl group, a C_{3-7} cycloalkenyl group, A heterocycle group (passage of said definition.), and C_{6-14} aryl C_{1-6} alkyl group, A C_{3-7} cycloalkyl C_{1-6} alkyl group and C_{3-7} cyclo alkenyl C_{1-6} alkyl group and a heterocycle C_{1-6} alkyl group (here, this basis) A C_{1-6} alkyl group replaced by heterocycle as said definition is shown. Are and here, This C_{6-14} aryl group, this C_{3-7} cycloalkyl group, this C_{3-7} cycloalkenyl group, A this heterocycle group and this C_{6-14} aryl C_{1-6} alkyl group, A this C_{3-7} cycloalkyl C_{1-6} alkyl group, a this C_{3-7} cyclo alkenyl C_{1-6} alkyl group, and this heterocycle C_{1-6} alkyl group, It may be replaced by 1 thru/or 3 substituents chosen from the following group C, When this substituent is two pieces or three pieces, that a substituent is the same respectively or a {group C:halogen atom which may differ, it is, even if replaced by a substituent chosen from the above-mentioned group A -- a C_{1-6} alkyl group and -OR^{c1} (R^{c1} is a hydrogen atom or a C_{1-6} alkyl group among a formula.) -- and, - $NR^{c2}R^{c3}$ (among a formula, respectively, or it differs and R^{c2} and R^{c3} are a hydrogen atom or a C_{1-6} alkyl group.). }.]. }. The ring Cy A C_{6-14} aryl group, a C_{3-7} cycloalkyl group, Or are a heterocycle group (passage of said definition.) and this C_{6-14} aryl group, this C_{3-7} cycloalkyl group, and this heterocycle group, when it may be replaced by 1 thru/or 3 substituents chosen from the above-mentioned group B and this substituent is two pieces or three pieces, a substituent is the same respectively -- or it may differ.]

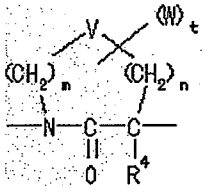
[0015](2) The salt permitted on a thiazole compound expressed with following general formula [II], or medicine manufacture.

[Formula 15]



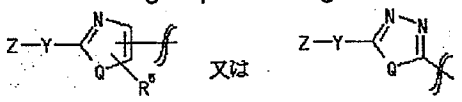
[II]

R^1 among [type A hydrogen atom, a halogen atom, Are a C_{1-6} alkyl group and R^2 Or a hydrogen atom, Or it is a C_{1-6} alkyl group which may be replaced by the substituent chosen from the following group A, and they are a {group A:halogen atom and $-OR^{b1}$ (R^{b1} among a formula). they are a hydrogen atom or a C_{1-6} alkyl group $-SR^{b2}$ (the inside of a formula, and R^{b2} -- a hydrogen atom.) or it is a C_{1-6} alkyl group -- and $-NR^{b3}R^{b4}$ (R^{b3} and R^{b4} among a formula) same respectively or differing -- a hydrogen atom and a C_{1-6} alkyl group. Or the heterocycle group which is a heterocycle group which becomes together with the nitrogen atom in which R^{b3} and R^{b4} adjoin, and is formed, becomes together with the nitrogen atom which this adjoins here, and is formed, Besides one nitrogen atom, it may be replaced by a C_{1-6} alkyl group including 0 thru/or 3 hetero atoms chosen from an oxygen atom, a nitrogen atom, or a sulfur atom. . }R^3 and R^4 are the same respectively, or differ from each other, The C_{1-6} alkyl group, $-OR^{a1}$ (R^{a1} among a formula) which may be replaced by the substituent chosen from a hydrogen atom and the above-mentioned group A they are a hydrogen atom, a C_{1-6} alkyl group, or a C_{1-6} alkyl carbonyl group. Or the inside of a $-NR^{a2}R^{a3}$ {type, R^{a2}, and R^{a3}, It is a heterocycle group (passage of said definition.) which becomes together with the nitrogen atom in which it differs and a hydrogen atom, a C_{1-6} alkyl group, a C_{1-6} alkoxycarbonyl group or R^{a2}, and R^{a3} adjoin respectively identically, and is formed. It is} and R^2 and R^3 become together with adjoining $-N-CO-CR^4-$, [Formula 16]



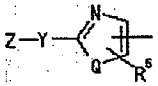
{V among a formula $-CH_2-$, -O-, -S-, -CO-, -OCO-, $-NR^{a5}-$, $-CO-NR^{a5}-$, Or $-NR^{a5}-CO$ - (here, R^{a5}) A hydrogen atom, C_{1-6} alkyl group, and C_{6-14} aryl C_{1-6} alkyl group, a C_{1-6} alkoxycarbonyl group, Or it is a C_{6-14} aryl C_{1-6} alkyloxy carbonyl group. W C_{1-6} alkyl group, or when it is a substituent chosen from the above-mentioned group A, t is 0, 1, or 2 and t is 2, two W is the same respectively – or it may differ and m and n are the same respectively -- or it differs and is an integer of 0, or 1 thru/or 3. May form a ring expressed with} and X A single bond, C_{1-4}

alkylene, -O-, -S-, -COO-, -OCO-, -NR^{a4}-, -CO-NR^{a4}-, Or it is -NR^{a4}-CO- (R^{a4} is a C_{1-6} alkyl group which may be replaced by hydrogen atom or a substituent chosen from the above-mentioned group A among a formula.), [0016]Ring Hy',[Formula 17]



{-- here -- Q -NR^{a6}- (the inside of a formula, and R^{a6} -- a hydrogen atom.) or it is a C_{1-6} alkyl group which may be replaced by a substituent chosen from the above-mentioned group A. Are -O- and -S- and R^5 Or a hydrogen atom, a halogen atom, Or are a C_{1-6} alkyl group and Y, A single bond, -CH=CH-, -O-, -CH(OH)-, -COO-, - NR^{b5}-, -NR^{b6}-CO-, -NR^{b7}-COO-, - NR^{b8}-CO-NR^{b9}-, -NR^{b10}-SO_2-, and -CO-NR^{b11}- (the inside of a formula, and R --) [^{b5} and] R^{b6}, R^{b7}, R^{b8}, R^{b9}, R^{b10}, and R^{b11} A hydrogen atom, Or it is a C_{1-6} alkyl group. Z, A hydrogen atom, a C_{1-6} alkyl group which may be replaced by a substituent chosen from the above-mentioned group A, A C_{6-14} aryl group, C_{3-7} cycloalkyl group, C_{3-7} cycloalkenyl group, heterocycle group (passage of said definition.), and C_{6-14} aryl C_{1-6} alkyl group, A C_{3-7} cycloalkyl C_{1-6} alkyl group and C_{3-7} cyclo alkenyl C_{1-6} alkyl group and a heterocycle C_{1-6} alkyl group (here, this basis) A C_{1-6} alkyl group replaced by heterocycle as said definition is shown. Are and here, This C_{6-14} aryl group, this C_{3-7} cycloalkyl group, this C_{3-7} cycloalkenyl group, A this heterocycle group and this C_{6-14} aryl C_{1-6} alkyl group, A this C_{3-7} cycloalkyl C_{1-6} alkyl group, a this C_{3-7} cyclo alkenyl C_{1-6} alkyl group, and this heterocycle C_{1-6} alkyl group, It may be replaced by 1 thru/or 3 substituents chosen from the following group C, When this substituent is two pieces or three pieces, that a substituent is the same respectively or a {group C:halogen atom which may differ, It is, even if replaced by a substituent chosen from the above-mentioned group A, and they are a C_{1-6} alkyl group and -OR^{c1} (R^{c1} among a formula). they are a hydrogen atom or a C_{1-6} alkyl group -- and -$NR^{c2}R^{c3}$ (among a formula, R^{c2} and R^{c3} are the same respectively, or it differs and a hydrogen atom.) Or it is a C_{1-6} alkyl group. . }.]. }. The ring Cy A C_{6-14} aryl group, a C_{3-7} cycloalkyl group, Or are a heterocycle group (passage of said definition.) and this C_{6-14} aryl group, this C_{3-7} cycloalkyl group, and this heterocycle group, when it may be replaced by 1 thru/or 3 substituents chosen from the following group B and this substituent is two pieces or three pieces, a substituent is the same respectively -- or it may differ.

{group B: A nitro group, a halogen atom, and -Y-Z(Y and Z passage of said definition.)}]
[0017](3) Ring Hy', [Formula 18]



(-- the inside of a formula, and each sign -- the passage according to claim 2.) -- it is -- the salt permitted on a thiazole compound given in (2), or medicine manufacture.
[0018](4) The salt with which Y is permitted on the thiazole compound given in (3) which is -NR^{b5}- or -NR^{b6}-CO- (the inside of a formula, and each sign the passage according to claim 2.), or medicine manufacture.
[0019](5) The salt with which Q is permitted on the thiazole compound given in (4) which is -S-, or medicine manufacture.
[0020](6) The salt with which X is permitted on the thiazole compound given in (5) which is a single bond, or medicine manufacture.
[0021](7) The salt permitted on the thiazole compound given [given Y is -NR^{b6}-CO- (inside of a formula, and sign R^{b6} the passage according to claim 2.)] in (6) given Z is a C_{1-6} alkyl group or a C_{3-7} cycloalkyl group, or medicine manufacture.
[0022](8) The ring Cy is the salt permitted on a thiazole compound given in (7) which is a phenyl group or a pyridyl group, or medicine manufacture, and phenyl group concerned and a pyridyl group, when it may be replaced by 1 thru/or 3 substituents chosen from the group C according to claim 2 and this substituent is two pieces or three pieces, this substituent is the same respectively -- or it may differ.
[0023](9) A medicinal composition containing the salt permitted on a thiazole compound (2) thru/or given in (8), or medicine manufacture.
[0024](10) A proteinkinase C isozyme gamma selective inhibition agent containing the salt permitted on a thiazole compound (1) thru/or given in (9), or medicine manufacture.
[0025](11) A painkiller containing the salt permitted on a thiazole compound (2) thru/or given in (9), or medicine manufacture.
[0026]Each definition used in this specification is as follows. "Proteinkinase C inhibitor" is drugs which treat or/and prevent condition relevant to PKC by checking the enzyme activity of proteinkinase C (the following, PKC). hurting as a condition relevant to PKC (a pain, a hyperalgesia, and allodynia.) diabetic complications (diabetic retinopathy.), such as tolerance over narcotic analgesics, such as morphine Arteriosclerosis and angiopathies, such as diabetic nephropathy, diabetic cardiomyopathy, and a diabetic neuropathy, inflammation (thrombosis etc.), a dermatosis, immune diseases (acquired immunodeficiency etc.), central nervous system diseases (Alzheimer disease etc.), cancer, etc. are mentioned. "Proteinkinase C

isozyme gamma selective inhibition agents" is drugs which check the enzyme activity of gamma in a PKC isozyme, and what has high inhibiting activity over gamma is preferred especially as compared with other isozymes and inhibiting activity over alpha and beta. Especially preferably, the inhibiting activity of gamma is a thing of 3 times or more of alpha and beta, and a 10 or more time thing is still more preferred. "Painkillers" is drugs which reduce or vanish a pain, and what suppresses a pain which happens especially by pain, intense pains, such as a postoperative pain, or nervous damage, a functional disorder, etc. is preferred. Drugs which heighten an analgesic effect of an analgesic by the improvement of tolerance to narcotic analgesics which treat condition of abnormalities in a sensory nerve, such as a hyperalgesia and allodynia, such as drugs and morphine, are meant. Use of drugs for preventing these condition is included.

[0027]A "halogen atom" is a fluorine atom, a chlorine atom, a bromine atom, or iodine atoms, and is a fluorine atom, a chlorine atom, or a bromine atom preferably. In R^1, it is a chlorine atom especially preferably, and a fluorine atom especially preferably as a substituent (group B) of the ring Hy, a substituent (group C) of Z of the ring Hy, a substituent (group B) of the ring Cy, and a substituent (group C) of Z of the ring Cy.

[0028]A "C_{1-6} alkyl group" expresses a straight chain or a branched chain alkyl group of the carbon numbers 1 thru/or 6, and specifically, A methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group, an isopentyl group, a tert-pentyl group, a hexyl group, etc. are mentioned. Are a straight chain or a branched chain alkyl group of the carbon numbers 1 thru/or 4 preferably, and R^1, R^5, R^{a1}, R^{a2}, R^{a3}, In R^{b1}, R^{b2}, R^{b6}, R^{b7}, R^{b8}, R^{b9}, R^{b10}, R^{b11}, and W, preferably especially, It is a methyl group, and in R^{b3} and R^{b4}, it is a methyl group or an ethyl group, and is a methyl group still more preferably. In R^{a5}, it is a methyl group, an ethyl group, an isopropyl group, or an isobutyl group especially preferably, and is a methyl group still more preferably. In R^{b5} of the ring Hy, it is a methyl group or an ethyl group, is a methyl group preferably in R^{c1} of the ring Hy especially preferably, and a methyl group especially preferably in R^{b5} of the ring Cy, R^{c1}, R^{c2}, and R^{c3}.

[0029]A "C_{1-6} alkyl carbonyl group" is a carbonyl group which the above "C_{1-6} alkyl group" replaced, and, specifically, an acetyl group, a propionyl group, a butyryl group, an isobutyryl group, a pivaloyl group, etc. are mentioned. An alkylated site is a straight chain or a branched chain alkyl group of the carbon numbers 1 thru/or 4 preferably, and it is an acetyl group especially preferably in R^{a1}.

[0030]With a "C_{1-6} alkoxycarbonyl group." Alkyl of a C_{1-6} alkoxy part is an alkyloxy carbonyl

group which is the above "C_{1-6} alkyl group", A methoxycarbonyl group, an ethoxycarbonyl group, a carbopropoxy group, An isopropyl oxycarbonyl group, a butoxycarbonyl group, an isobutyloxy carbonyl group, a tert-butoxycarbonyl group, a pentyloxy carbonyl group, a hexyloxy carbonyl group, etc. are mentioned. An alkylated site is a straight chain or a branched chain alkyl group of the carbon numbers 1 thru/or 4 preferably, and it is a tert-butoxycarbonyl group especially preferably in R^{a2} and R^{a3}.

[0031]Including 0 thru/or 3 hetero atoms chosen from an oxygen atom, a nitrogen atom, or a sulfur atom besides one nitrogen atom, "a heterocycle group which becomes together with an adjoining nitrogen atom and is formed" is the heterocycle of saturation of 3 thru/or 10 membered-rings, or an unsaturation, and may be replaced by a C_{1-6} alkyl group. Specifically An aziridinyl group, a pyrrolyl group, a pylori nil group, a pyrrolidinyl group, An imidazolyl group, a pyrazolyl group, an oxazolyl group, a piperidino group, a piperazinyl group, a PIRAZORIJINIRU group, a morpholino group, an indolyl group, an isoindolyl group, an indri nil group, an isoindri nil group, a 4-methylpiperazine-1-yl group, etc. are mentioned. Preferably, besides one nitrogen atom, including 0 or one hetero atom chosen from an oxygen atom, a nitrogen atom, or a sulfur atom, it is the heterocycle of saturation of 5 or 6 membered-rings, or an unsaturation, and may be replaced by a C_{1-6} alkyl group. R^{b3} and R^{b4} preferably especially as "an adjoining heterocycle group which becomes together, becomes together with a nitrogen atom, and is formed", It is a pyrrolidinyl group, an imidazolyl group, a piperidino group, a morpholino group, and a 4-methyl-1-piperazinyl group, and R^{a2} and R^{a3} are piperidino groups especially preferably as "an adjoining heterocycle group which becomes together, becomes together with a nitrogen atom, and is formed."

[0032]A "C_{1-6} alkyl group" of the above-mentioned definition may be replaced by 1 thru/or 3 substituents chosen from the following group A, and "a C_{1-6} alkyl group which may be replaced by a substituent chosen from the group A" also contains an unreplaced C_{1-6} alkyl group. the group A -- a "halogen atom" of the above-mentioned definition, and $-OR^{b1}$ (the inside of a formula, and R^{b1} -- a hydrogen atom.) or it is the "C_{1-6} alkyl group" of the above-mentioned definition $-SR^{b2}$ (the inside of a formula, and R^{b2} -- a hydrogen atom.) or it is the "C_{1-6} alkyl group" of the above-mentioned definition -- and $-NR^{b3}R^{b4}$ (R^{b3} and R^{b4} among a formula) respectively, or it differs and a hydrogen atom, a "C_{1-6} alkyl group" of the above-mentioned definition or R^{b3}, and R^{b4} are "the heterocycle groups which becomes together with an adjoining nitrogen atom and is formed" of the above-mentioned definition. it is . As a C_{1-6} alkyl

group which may be replaced by a substituent chosen from this group A, specifically, A methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, A sec-butyl group, a tert-butyl group, a pentyl group, an isopentyl group, A tert-pentyl group, a hexyl group, a chloromethyl group, a trifluoromethyl group, 2-hydroxyethyl group, 3-hydroxypropyl group, a 2-methoxy ethyl group, 2-methylthio ethyl group, 2-aminoethyl, 2-(methylamino) ethyl group, 2-(dimethylamino) ethyl group, 2-(diethylamino) ethyl group, 3-(dimethylamino) propyl group, 4-(dimethylamino) butyl group, 3-(dimethyl aminomethyl) butyl group, 1-(dimethyl aminomethyl) butyl group, 2-piperidino ethyl group, 2-(piperazine 1-yl) ethyl group, 3-(4-methylpiperazine-1-yl) propyl group, 2-morpholino ethyl group, 3-(imidazoline 1-yl) propyl group, 2-(pyrrolizine-1-yl) ethyl group, etc. are mentioned.

[0033]In R^2, it is the "C_{1-6} alkyl group" of no replacing, $-OR^{b1}$ substitution, or $-NR^{b3}R^{b4}$ substitution (passage of the above [each sign].) preferably, Specifically A methyl group, 2-hydroxyethyl group, 3-hydroxypropyl group, A 2-methoxy ethyl group, 2-aminoethyl, 2-(methylamino) ethyl group, 2-(dimethylamino) ethyl group, 2-(diethylamino) ethyl group, 3-(dimethylamino) propyl group, 4-(dimethylamino) butyl group, 2-piperidino ethyl group, 3-(4-methylpiperazine-1-yl) propyl group, Are 2-morpholino ethyl group, 3-(imidazoline 1-yl) propyl group, and 2-(pyrrolizine-1-yl) ethyl group, and in R^2 preferably especially, - Are the "C_{1-6} alkyl group" of $NR^{b3}R^{b4}$ substitution, and specifically, It is 2-aminoethyl, 2-(methylamino) ethyl group, 2-(dimethylamino) ethyl group, 2-(diethylamino) ethyl group, 3-(dimethylamino) propyl group, or 4-(dimethylamino) butyl group, and is 2-(dimethylamino) ethyl group still more preferably. In R^3, it is unreplaced a "C_{1-6} alkyl group" preferably, and is a methyl group especially preferably. In Z (group B) of the ring Hy, preferably, a methyl group, an ethyl group, an isopropyl group, an isobutyl group, a tert-butyl group, 3-pentyl group, a trifluoromethyl group, a hydroxymethyl group, a dimethyl aminomethyl group, or a methylthio methyl group -- they are a methyl group or a tert-butyl group especially preferably. In a substituent (group C) of Z of the ring Hy, they are a methyl group, a tert-butyl group, or a trifluoromethyl group preferably. In Z of the ring Cy, they are a methyl group, an isopropyl group, an isobutyl group, a tert-butyl group, a trifluoromethyl group, or a dimethyl aminomethyl group preferably. In a substituent (group C) of Z of the ring Cy, they are a methyl group, a propyl group, a tert-butyl group, and a trifluoromethyl group preferably.

[0034]"C_{1-4} alkylene" is the alkylene of a straight chain of the carbon numbers 1 thru/or 4, or branched chain, and methylene, ethylene, trimethylene, propylene, tetramethylen, etc. are mentioned. In X, it is methylene and ethylene preferably, and is methylene especially preferably.

[0035]A "C_{6-14} aryl group" is an aromatic hydrocarbon group of the carbon numbers 6 thru/or

14, and a phenyl group, a naphthyl group, an anthryl group, an azulenyl group, a phenan tolyl group, etc. are specifically mentioned. In Z (group B) of the ring Hy, and Z (group B) of the ring Cy and the ring Cy, it is a phenyl group or a naphthyl group preferably, and is a phenyl group especially preferably.

[0036]A "C_{3-7} cycloalkyl group" is a saturation cycloalkyl group of 3 thru/or 7 carbon numbers, and is specifically a cyclopropyl group, a cyclobutyl group, a cyclopentylic group, a cyclohexyl group, or a cycloheptyl group. As Z (group B) of the ring Cy and the ring Cy, preferably, It is a cyclopentylic group, a cyclohexyl group, and a cycloheptyl group, is a cyclohexyl group especially preferably in Z (group B) of the ring Cy and the ring Cy, and is a cyclopropyl group especially preferably in Z (group B) of the ring Hy.

[0037]Although, as for "C_{3-7} cycloalkenyl groups", 3 thru/or 7 carbon numbers are 5 thru/or 7 cycloalkenyl groups preferably and a partial double bond is included, an aryl group like a phenyl group and a cycloalkyl group of full saturation are not included. Specifically, a cyclopropenyl group, a cyclo butenyl group, a cyclopentenyl group, a cyclopentadienyl group, a cyclohexenyl group, 2,4-cyclohexadiene 1-yl groups, 2,5-cyclohexadiene 1-yl groups, a cycloheptenyl group, etc. are mentioned. In Z of the ring Hy, it is a cyclopentenyl group especially preferably.

[0038]A "heterocycle group" is a heterocycle group of saturation of a five-membered ring or six membered-rings, or an unsaturation containing 1 thru/or 4 hetero atoms chosen from an oxygen atom, a nitrogen atom, or a sulfur atom, and they condense with condensation or the benzene ring mutually, and may form a condensed ring of two rings. As a heterocycle group which is a monocycle, specifically A pyridyl group, a pyrazinyl group, A pyrimidinyl group, a pyridazinyl group, a thoriadinyl group, a pyrrolyl group, a pyrazolyl group, An imidazolyl group, a triazoryl group, a tetrazolyl group, a thienyl group, a furil group, An oxazolyl group, an isoxazolyl group, a thiazolyl group, an isothiazolyl group, An oxadiazolyl group, a thiadiazolyl group, a pylori nil group, a pyrrolidinyl group, an imidazolidinyl group, a piperidyl group, a piperazinyl group, a morphoryl group, a thio morphoryl group, a tetrahydropyranyl group, etc. are mentioned. As a heterocycle group which is a condensed ring, specifically, A quinolyl group, an isoquinolyl group, a chinae-cortex ZORINIRU group, a quinoxalinyl group, A phthalazinyl group, a SHINNORINIRU group, a NAFUCHIJINIRU group, a 5,6,7,8-tetrahydro quinolyl group, An indolyl group, a benzo imidazolyl group, a benzofuranyl group, a benzo thienyl group, A 1,3-dioxa indan nil group, a yne DONIRIRU group, a benzoxazolyl group, a benzothiazolyl group, a 1,3-dioxoiso indolyl group, a 1-oxo 1,2-dihydroisoquinolyl group, a 1-oxo 1,2,3,4-tetrahydro isoquinolyl group, etc. are mentioned.

[0039]Preferably, in the ring Hy, are an unsaturation heterocycle group which is a monocycle of 5 members or 6 members, and specifically, A pyridyl group, a pyrazinyl group, a pyrimidinyl group, a pyridazinyl group, a thoriadinyl group, A pyrrolyl group, a pyrazolyl group, an

imidazolyl group, a triazoryl group, a tetrazolyl group, a furil group, a thienyl group, an oxazolyl group, an isoxazolyl group, an oxadiazolyl group, a thiazolyl group, an isothiazolyl group, an oxadiazolyl group, a thiadiazolyl group, etc. are mentioned. Preferably especially A pyridyl group, a pyrrolyl group, a furil group, a thienyl group, An imidazolyl group, an oxazolyl group, an isoxazolyl group, a thiazolyl group, it is, and still more preferably, it is an isothiazolyl group, a triazoryl group, an oxadiazolyl group, or a thiadiazolyl group, and is [it comes out and / it is an oxazolyl group, a thiazolyl group, or a thiadiazolyl group and] a thiazolyl group most preferably. In Z (group B) of the ring Hy, it is a heterocycle group of an unsaturation or saturation which is a monocycle of 5 members or 6 members preferably, and, specifically, an imidazolyl group, a thienyl group, a pyrrolidinyl group, a piperidyl group, a morphoryl group, etc. are mentioned. Preferably, in the ring Cy, are a heterocycle group of an unsaturation or saturation or a condensed ring of them and the benzene ring which is a monocycle of 5 members or 6 members, and specifically, An imidazolyl group, a thienyl group, a pyrrolidinyl group, a piperidyl group, an indolyl group, a benzofuranyl group, a benzo thienyl group, a 1,3-dioxa indan nil group, etc. are mentioned. In Z (group B) of the ring Cy, preferably, Are a heterocycle group of an unsaturation or saturation or a condensed ring of them and the benzene ring which is a monocycle of 5 members or 6 members, and specifically, A pyrrolyl group, a furil group, a thienyl group, an imidazolyl group, an isoxazolyl group, A pyrrolidinyl group, a pyrazinyl group, a pyridyl group, a piperidyl group, a morphoryl group, an indolyl group, a benzofuranyl group, a benzo thienyl group, a 1,3-dioxa indan nil group, a quinolyl group, a quinoxalinyl group, a SHINNORINIRU group, etc. are mentioned. They are a pyridyl group, a pyrazinyl group, a pyrrolyl group, a furil group, a thienyl group, a pyrrolidinyl group, a morphoryl group, an isoxazolyl group, an indolyl group, a quinolyl group, a quinoxalinyl group, and a SHINNORINIRU group especially preferably.

[0040]With a "C_{6-14} aryl C_{1-6} alkyl group." It is the above "C_{1-6} alkyl group" which the above "C_{6-14} aryl group" replaced, an alkylated site is a straight chained alkyl group of the carbon numbers 1 thru/or 4 preferably, and an aryl part is an arylated alkyl group which is a phenyl group. Specifically, benzyl, a phenethyl group, 3-phenylpropyl group, 2-phenylpropyl group, 4-phenylbutyl group, etc. are mentioned. In Z (group B) of the ring Hy, and Z (group B) of the ring Cy, they are benzyl or a phenethyl group especially preferably.

[0041]A "C_{3-7} cycloalkyl C_{1-6} alkyl group" is a cycloalkyl alkyl group whose alkylated site it is the above "C_{1-6} alkyl group" which the above "C_{3-6} cycloalkyl group" replaced, and is a straight chained alkyl group of the carbon numbers 1 thru/or 4 preferably. Specifically A cyclopropyl methyl group, a cyclobutylmethyl group, a cyclopentylmethyl group, A cyclohexylmethyl group, a cycloheptyl methyl group, 2-cyclo propylethyl group, 2-cyclobutylethyl group, 2-cyclopentylethyl group, 2-cyclohexylethyl group, a 2-cycloheptyl ethyl group, etc. are

mentioned. They are a cyclopentylmethyl group or a cyclohexylmethyl group preferably as Z (group B) of the ring Hy.

[0042]A "C_{3-7} cyclo alkenyl C_{1-6} alkyl group" is a cyclo alkenyl alkyl group whose alkylated site it is the above "C_{1-6} alkyl group" which the above "C_{3-6} cycloalkenyl group" replaced, and is a straight chained alkyl group of the carbon numbers 1 thru/or 4 preferably. Specifically A methyl group (2-cyclopropene 1-yl), a methyl group (2-cyclobutene 1-yl), (2-cyclopentene 1-yl) A methyl group, 2-(2-cyclopentene 1-yl) ethyl group, (2,4-cyclopentadiene 1-yl) A methyl group, a methyl group (2-cyclohexenyl 1-yl), (3-cyclohexenyl 1-yl) A methyl group, a methyl group (2,4-cyclohexadiene 1-yl), a methyl group (2,5-cyclohexadiene 1-yl), a methyl group (2-cycloheptenyl), etc. are mentioned. In Z of the ring Hy, it is a methyl group (2-cyclopentene 1-yl) especially preferably.

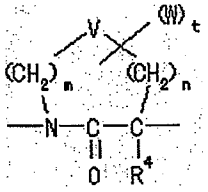
[0043]A "heterocycle C_{1-6} alkyl group" is the above "C_{1-6} alkyl group" which the above "heterocycle group" replaced, and is a heterocycle alkyl group whose heterocycle part is the monocyclic heterocycle of 5 members or 6 members and whose alkylated site is a straight chained alkyl group of the carbon numbers 1 thru/or 4 preferably. Specifically 1-pyrrolyl methyl group, 2-furil methyl group, 2-thienyl methyl group, 1-imidazolyl methyl group, 2-pyrrolidinyl methyl group, a 4-pyrazinyl methyl group, 4-pyridyl methyl group, a morpholino methyl group, etc. are mentioned, and they are 2-thienyl methyl group or 1-imidazolyl methyl group especially preferably in the ring Hy.

[0044]With a "C_{6-14} aryl C_{1-6} alkyloxy carbonyl group." A C_{6-14} aryl C_{1-6} alkylated site is an arylated alkyl oxycarbonyl group which is the above "C_{1-6} alkyl group" which the above "C_{6-14} aryl group" replaced, Preferably, a heterocycle part is the monocyclic heterocycle of 5 members or 6 members, and an alkylated site is a straight chained alkyl group of the carbon numbers 1 thru/or 4. Specifically, a benzyloxycarbonyl group, a phenethyloxy carbonyl group, 3-phenylpropyl oxycarbonyl group, 2-phenylpropyl oxycarbonyl group, 4-phenylbutyloxy carbonyl group, etc. are mentioned. In R^{a5}, it is a benzyloxycarbonyl group especially preferably.

[0045]Preferably as R^1, it is a hydrogen atom, a chlorine atom, or a methyl group, and is a hydrogen atom especially preferably. It is the above "C_{1-6} alkyl group which may be replaced by a substituent chosen from the group A" preferably as R^2, A methyl group, 2-hydroxyethyl group, 3-hydroxypropyl group, a 2-methoxy ethyl group, 2-aminoethyl group, 2-(methylamino) ethyl group, 2-(dimethylamino) ethyl group, 2-(diethylamino) ethyl group, 3-(dimethylamino) propyl group, 4-(dimethylamino) butyl group, 2-piperidino ethyl group, 2-(piperidine- 1-yl) ethyl group, 3-(4-methylpiperazine-1-yl) propyl group, 2-morpholino ethyl group, 3-(imidazoline 1-yl) propyl group, 2-(pyrrolizine-1-yl) ethyl group, etc. are mentioned. Preferably especially 2-

aminoethyl group, 2-(methylamino) ethyl group, It is 2-(dimethylamino) ethyl group, 2-(diethylamino) ethyl group, 3-(dimethylamino) propyl group, or 4-(dimethylamino) butyl group, and is 2-(dimethylamino) ethyl group still more preferably.

[0046]It is a hydrogen atom preferably as R^3. Become together with -N-CO-CR^4- which R^2 and R^3 adjoin. [Formula 19]



(-- passage of the above [the inside of a formula, and each sign].) -- it is also preferred to form the ring expressed. Here, V has -CO- or preferred -NR^{a5}- (here, passage of the above [R^{a5}].), and especially its -NR^{a5}- is preferred. When V is -NR^{a5}-, it is a C_{1-6} alkyl group preferably as R^{a5}, and especially a methyl group is preferred. Differ, it is desirable especially preferred identically [respectively] that it is 0, 1, or 2, and m and n are m+n=1 or m+n=2. When V is -CO-, m= 0 and especially n= 1 are preferred, and when V is -NR^{a5}-, m= 2 and especially n= 0 are preferred. It is a hydrogen atom preferably as R^4. Preferably as X, it is a single bond or C_{1-4} alkylene, and is a single bond especially preferably.

[0047]It is an unsaturation heterocycle group which is a monocycle of 5 members or 6 members preferably as the ring Hy. they are specifically a pyridyl group, a pyrrolyl group, a furil group, a thienyl group, an imidazolyl group, an oxazolyl group, an isoxazolyl group, a thiazolyl group, an isothiazolyl group, a triazoryl group, an oxadiazolyl group, or a thiadiazolyl group -- especially -- desirable [Formula 20]

(-- passage of the above [the inside of a formula, and each sign].) -- it is . It is an oxazolyl group, a thiazolyl group, or a thiadiazolyl group, and is a thiazolyl group most preferably. As for the ring Hy, it is preferred to replace by the 4th place of the thiazolyl group of a general formula, and when the ring Hy is a thiazolyl group, replacing by the 5th place is preferred. Preferably as R^5, it is the above "C_{1-6} alkyl group", and is a methyl group especially preferably.

[0048]Preferably as a substituent (group B) of the ring Hy, it is the above "halogen atom" or -Y-Z, and is -Y-Z especially preferably. As for the ring Hy, it is preferred to be replaced by 1 or two

-Y-Z. As for one of them, when -Y-Z is two pieces as a substituent (group B) of the ring Hy, Y is a single bond and it is preferred that Z is the above "C_{1-6} alkyl group which may be replaced by the substituent chosen from the group A." Especially preferably, it is a methyl group or a hydroxymethyl group, and is a methyl group still more preferably. As a substituent (group B) of the ring Hy, at least one -Y-Z, Y A single bond, -O-, -COO-, $-NR^{b5}-$, $-NR^{b6}-CO-$, $-NR^{b7}-COO-$, Or it is preferred that it is $-NR^{b10}-SO_2-$ (passage of the above [the inside of a formula and each sign].), Z A hydrogen atom, the above "C_{1-6} alkyl group which may be replaced by the substituent chosen from the group A", The above "C_{6-14} aryl group", the above "C_{3-7} cycloalkyl group", The above "heterocycle group", the above "C_{6-14} aryl C_{1-6} alkyl group", It is preferred that they are the above "C_{3-7} cycloalkyl C_{1-6} alkyl group", the above "C_{3-7} cyclo alkenyl C_{1-6} alkyl group", and the above "heterocycle C_{1-6} alkyl group." Especially preferably as Y, it is $-NR^{b5}-$ or $-NR^{b6}-CO-$ and is $-NR^{b6}-CO-$ still more preferably. Here, it is a hydrogen atom preferably as R^{b5}, R^{b6}, R^{b7}, and R^{b10}. Preferably as Z especially A hydrogen atom, the above "C_{1-6} alkyl group which may be replaced by the substituent chosen from the group A", Or it is the above "C_{3-7} cycloalkyl group", and still more preferably, it is the above "C_{1-6} alkyl group which may be replaced by the substituent chosen from the group A", or the above "C_{3-7} cycloalkyl group", and they are a methyl group or a cyclopropyl group most preferably. This C_{6-14} aryl group, this C_{3-7} cycloalkyl group, A this C_{3-7} cycloalkenyl group, this heterocycle group, and this C_{6-14} aryl C_{1-6} alkyl group, A this C_{3-7} cycloalkyl C_{1-6} alkyl group, a this C_{3-7} cyclo alkenyl C_{1-6} alkyl group, and this heterocycle C_{1-6} alkyl group, when it may be replaced by 1 thru/or 3 substituents chosen from the following group C and this substituent is two pieces or three pieces, a substituent is the same respectively -- or it may differ.Group C: The above "halogen atom", the above "C_{1-6} alkyl group which may be replaced by the substituent chosen from the group A", $-OR^{c1}$ (R^{c1} among a formula) they are a hydrogen atom or the above "C_{1-6} alkyl group" -- and $-NR^{c2}R^{c3}$ (among a formula, respectively, or it differs and R^{c2} and R^{c3} are a hydrogen atom or the above "C_{1-6} alkyl group".) As a substituent (group C) of Z of the ring Hy, preferably, It is, even if replaced by the substituent chosen from above-mentioned "halogen atom" above-mentioned "group A, and it is C_{1-6} alkyl group" or $-OR^{c1}$, and they are a fluorine atom, a methyl group, a tert-butyl group, a trifluoromethyl group, or a methoxy group still more preferably. When the substituent of the ring Hy is -Y-Z, in $-NR^{b5}-$ and R^{b5}, a

hydrogen atom and Z the desirable combination of Y and Z A hydrogen atom, [Y] Or in Y, -NR^{b6}-CO- and R^{b6} are [a hydrogen atom and Z] the above "C_{1-6} alkyl group which may be replaced by the substituent chosen from the group A", or the above "C_{3-7} cycloalkyl group."

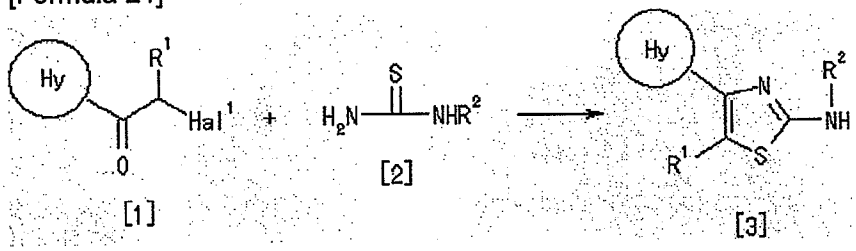
[0049]Preferably as the ring Cy, are the above "C_{6-14} aryl group" or a "heterocycle group", and preferably especially, It is a phenyl group, a pyridyl group, an imidazolyl group, a thienyl group, a pyrrolidinyl group, a piperidyl group, an indolyl group, a benzofuranyl group, a benzo thienyl group, and a 1,3-dioxa indan nil group, and is a phenyl group still more preferably. As for the ring Cy, it is preferred that they are no replacing or 1 substitution, and as for a substituent (group B) of the ring Cy, when the ring Cy is a phenyl group, it is preferred that it is the 2nd place. Preferably as a substituent (group B) of the ring Cy, it is the above "halogen atom" and is a fluorine atom especially preferably. When a substituent (group B) of the ring Cy is -Y-Z, as Y preferably, A single bond, -CH=CH-, -O-, -C(OH)-, -NR^{b5}-, - NR^{b6}-CO-, -NR^{b8}-CO-NR^{b9}-, - It is NR^{b10}-SO_2- and -CO-NR^{b11}- (each sign is as aforementioned among a formula.), and they are a single bond, -O-, and -NR^{b6}-CO- especially preferably. Here, preferably as R^{b5}, R^{b6}, R^{b8}, R^{b10}, and R^{b11}, it is a hydrogen atom and a methyl group preferably as R^{b9}. When a substituent (group B) of the ring Cy is -Y-Z, as Z preferably, A hydrogen atom, the above "C_{1-6} alkyl group which may be replaced by a substituent chosen from the group A", The above "C_{6-14} aryl group", the above "C_{3-7} cycloalkyl group", the above "heterocycle group", Or are the above "C_{6-14} aryl C_{1-6} alkyl group", and preferably especially, A hydrogen atom, a methyl group, an isopropyl group, an isobutyl group, a tert-butyl group, A trifluoromethyl group or a dimethyl aminomethyl group, a phenyl group, a cyclopentylic group, They are a cyclohexyl group, a cycloheptyl group, a pyrrolyl group, a furil group, a thienyl group, an isoxazolyl group, a pyrrolidinyl group, a pyridyl group, a pyrazinyl group, a piperidyl group, a morphoryl group, an indolyl group, a quinolyl group, a quinoxalinyl group, and a SHINNORINIRU group. This C_{6-14} aryl group, this C_{3-7} cycloalkyl group, A this C_{3-7} cycloalkenyl group, this heterocycle group, and this C_{6-14} aryl C_{1-6} alkyl group, A this C_{3-7} cycloalkyl C_{1-6} alkyl group, a this C_{3-7} cyclo alkenyl C_{1-6} alkyl group, and this heterocycle C_{1-6} alkyl group, when it may be replaced by 1 thru/or 3 substituents chosen from the above-mentioned group C and this substituent is two pieces or three pieces, a substituent is the same respectively -- or it may differ. They are a fluorine atom, a chlorine atom, a bromine atom, a methyl group, a propyl group, a tert-butyl group, a trifluoromethyl group, a methoxy group, an amino group, or a dimethylamino group preferably as a substituent (group C) of Z of the ring Cy.

[0050]In -Y-Z of ring Hy', a desirable mode is the same as the ring Hy.
[0051]As long as "the salt permitted on medicine manufacture" forms a compound shown by the above-mentioned general formula [I], and a nonpoisonous salt, what kind of salt may be sufficient as it, For example, inorganic acid; or oxalic acid, such as chloride, sulfuric acid, phosphoric acid, and hydrobromic acid, Malonic acid, citrate, fumaric acid, lactic acid, malic acid, succinic acid, tartaric acid, Organic acid; or sodium hydroxide, such as acetic acid, gluconic acid, ascorbic acid, methylsulfonic acid, and benzylsulfonic acid, Inorganic base; or methylamines, such as a potassium hydrate, calcium hydroxide, magnesium hydroxide, and ammonium hydroxide, It can obtain by making it react to amino acid, such as organic base [, such as diethylamine, triethylamine, triethanolamine, ethylenediamine, tris(hydroxymethyl) methylamine, guanidine, Kolin, and cinchonine]; or lysine, arginine, and an alanine. As for a hydrate and solvate, hydrated compound ****** of each compound is included in this invention.
[0052]Various isomers exist in a compound shown by the above-mentioned general formula [I]. For example, when E object and Z body exist as geometric isomer and an asymmetric carbon atom exists, mirror image isomer and diastereomer as a stereoisomeric form based on these exist. A tautomer may exist depending on the case. Therefore, these all isomers and those mixtures are included by the range of this invention.
[0053]A prodrug and metabolite of each compound are also included in this invention. A "prodrug" is a derivative of this invention compound in which it restores to the original compound and original drug effect is shown after having a basis which may be decomposed chemically or metabolically and medicating a living body, and a complex and a salt by a covalent bond are included.
[0054]A carrier permitted on publicly known medicine manufacture usually in itself when using this invention compound as medicinal preparation, An excipient, a diluent, an extender, disintegrator, stabilizer, a preservative, a buffer, an emulsifier, An aromatic, colorant, a sweetening agent, a viscous agent, corrigent, a solubilizing agent, other additive agents, Specifically Alcohol, such as water, vegetable oil, ethanol, or benzyl alcohol, It mixes with carbohydrates, such as a polyethylene glycol, glycerol triacetate, gelatin, lactose, and starch, magnesium stearate, talc, lanolin, vaseline, etc., systemic by making with a conventional method with a gestalt of a tablet, a pill, powder medicine, granulation, suppositories, injections, ophthalmic solutions, liquids and solutions, a capsule, trochiscus, aerosols, elixirs, suspension, an emulsion, syrups, etc. -- being certain -- it is -- local -- taking orally -- or it is parenteral and a medicine can be prescribed for the patient. Although a dose changes with age, weight, condition, a curative effect, medication methods, etc., it is the range of 0.1 mg thru/or 1 g, and 1 time per one adult is usually medicated with 1 time per thru/or several times day.
[0055]
[Embodiment of the Invention]Next, an example of the manufacturing method of the compound

used in order to carry out this invention is explained. However, the manufacturing method of this invention compound is not limited to these. What is necessary is just to manufacture efficiently by the device of replacing an order of each process and the process of introducing a protective group into a functional group if needed, and performing deprotection by a post process, even if unstated to this process. What is necessary is for what is necessary to be just to perform reaction processing by the method usually performed, and just to perform it in each process, by choosing suitably the method by which isolation refining, crystallization, recrystallization, silica gel chromatography, preparative isolation HPLC, etc. are used commonly, and combining it.

[0056]An one to one process process is a method of obtaining an amino substitution thiazole compound from alpha-halo ketone compound and a thiourea compound.

[Formula 21]

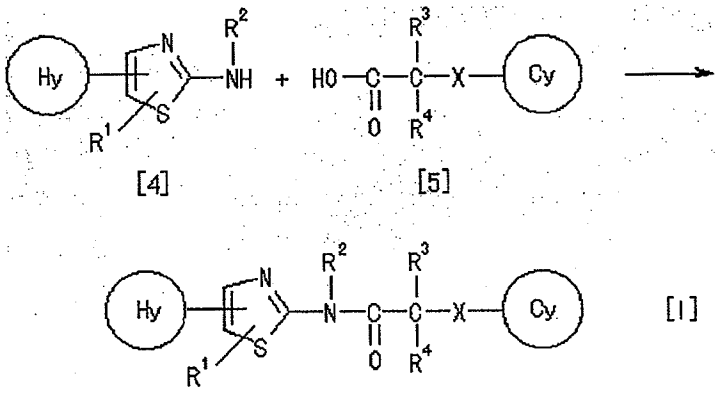


(Hal^1 being halogen atoms, such as a bromine atom and a chlorine atom, among a formula in addition passage of the above [each sign].)

An amino substitution thiazole compound [3] can be obtained by making alpha-halo ketone compound [1] obtained by the conventional method or the following process 2 react to the thiourea compound [2] obtained by the conventional method or the following process 3 among a solvent. As a desirable solvent, ether system solvent; methanol, such as dioxane and a tetrahydrofuran, Alcoholic solvent, such as ethanol; Dimethylformamide, dimethyl sulfoxide, Ester solvent [, such as hydrocarbon system solvent; ethyl acetate, such as; benzene and toluene, and butyl acetate], such as halogen system solvents, such as polar-solvent; dichloromethanes, such as acetonitrile and acetone, and chloroform; water or those mixed solvents are mentioned. As for a compound [1] and a compound [2], it is preferred to mix under ice-cooling and to make it react under a room temperature thru/or heating. Bases, such as potassium carbonate and sodium hydroxide, may be added.

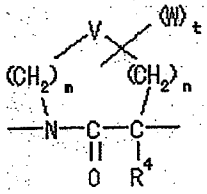
[0057]An one to two process process is a method of obtaining a thiazole compound expressed with general formula [I], by carrying out amide condensation of an amino substitution thiazole and the carboxylic acid compound.

[Formula 22]



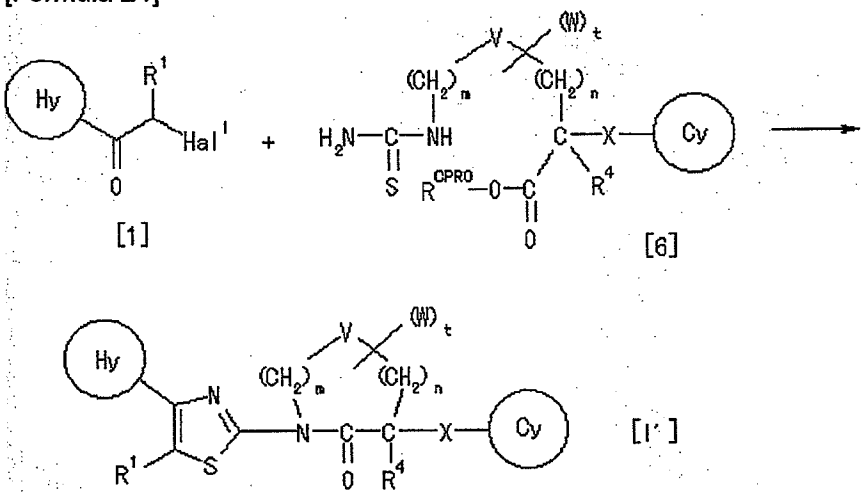
(Passage of the above [the inside of a formula, and each sign].)
Thiazole compound [I] can be obtained by carrying out amide condensation of the amino substitution thiazole compound [4] produced by making it be the same as that of a conventional method or the process 1-1 with the carboxylic acid compound [5] obtained by a conventional method. What is necessary is just to perform amide condensation with a conventional method, and a compound [4] DMF, Acetonitrile, THF, chloroform, ethyl acetate, a methylene chloride, The inside of solvents, such as toluene, dicyclohexylcarbodiimide, and a 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide and a hydrochloride, Thiazole compound [I] can be obtained by adding N-hydroxysuccinimide, 1-hydroxybenzotriazol, etc. [, such as diphenyl phosphoryl azide, / a condensing agent and if needed], and condensing with a carboxylic acid compound [5]. a carboxylic acid compound [5] being made into the acid halide derived by a thionyl chloride, chloridation OGIZARIRU, etc., or, Consider it as activation ester of a compound [5] by considering it as the mixed acid anhydride derived by pivaloyl chloride, chloroethyl carbonate, etc., and it ranks second, Thiazole compound [I] can also be obtained by making it react under existence of bases, such as triethylamine, potassium carbonate, and pyridine, or in amine solvents, such as pyridine, among solvents, such as DMF, acetonitrile, THF, chloroform, ethyl acetate, a methylene chloride, and toluene. It is desirable to perform this reaction under heating.

[0058]An one to three process process should become together with -N-CO-CR^4- which R^2 and R^3 adjoin in general formula [I]. [Formula 23]



(-- passage of the above [the inside of a formula, and each sign].) -- it is the method of obtaining the thiazole compound in the case of forming.

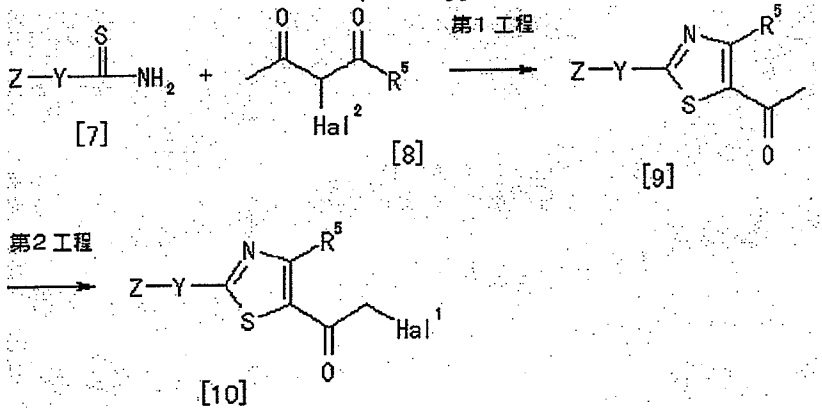
[Formula 24]



(R^{CPRO} is a protective group of carboxylic acid, such as a methyl group and an ethyl group, among a formula, in addition each sign is as aforementioned, and $-(W)_t-$ is a substituent on $-(CH_2)_m-V-(CH_2)_n-$ here.)

A compound [I'] can be obtained by making alpha-halo ketone compound [1] obtained by conventional method or the following process 2 react to a thiourea compound [6] preferably obtained by the following process 3 the bottom of heating, and among a solvent under a room temperature thru/or heating. As a desirable solvent, ether system solvent; methanol, such as dioxane and a tetrahydrofuran, Alcoholic solvent, such as ethanol; Dimethylformamide, dimethyl sulfoxide, Ester solvent [, such as hydrocarbon system solvent; ethyl acetate, such as; benzene and toluene, and butyl acetate], such as halogen system solvents, such as polar-solvent; dichloromethanes, such as acetonitrile and acetone, and chloroform; water or those mixed solvents are mentioned.

[0059]A two process process is a method of obtaining alpha-halo ketone compound as an intermediate of thiazole compound [I]. Process 2-1 [Formula 25]



(Hal^2 is halogen atoms, such as a chlorine atom and a bromine atom, among a formula, and each sign is as aforementioned.)

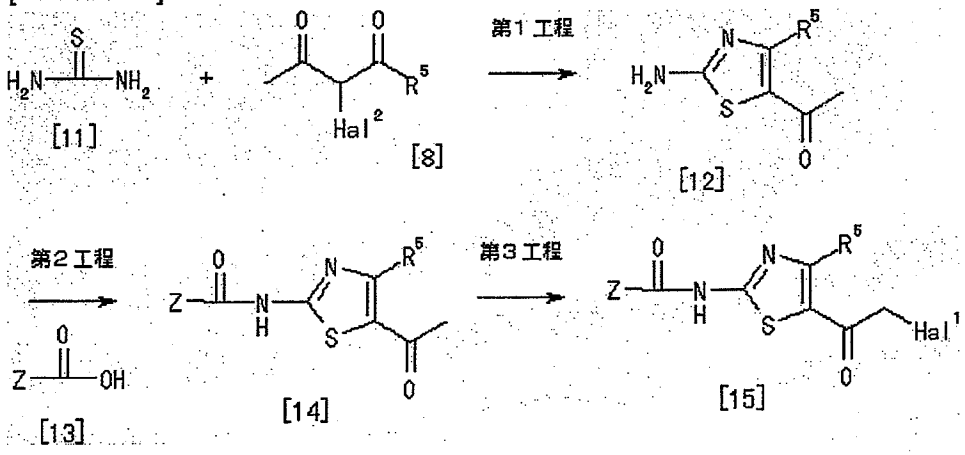
A compound [9] can be obtained by carrying out ring closure of the thioamide compound [7] obtained by the 1st process conventional method to a diketone compound [8] under heating preferably under a room temperature thru/or heating among solvents, such as methanol and ethanol. Bases, such as potassium carbonate and sodium hydroxide, may be added. As a desirable solvent, ether system solvent; methanol, such as dioxane and a tetrahydrofuran, Alcoholic solvent, such as ethanol; Dimethylformamide, dimethyl sulfoxide, Ester solvent [, such as hydrocarbon system solvent; ethyl acetate, such as; benzene and toluene, and butyl acetate], such as halogen system solvents, such as polar-solvent; dichloromethanes, such as acetonitrile and acetone, and chloroform; water or those mixed solvents are mentioned. A compound [9] is also compoundable like the following reference etc.

Reference: Khim Geterotsikl Soedin, 1995 (1), 130-132 (1995). Khim Geterotsikl Soedin, 1994 (2), 249-252 (1994). Indian J.Chem., 32 (8), 848-857 (1993).

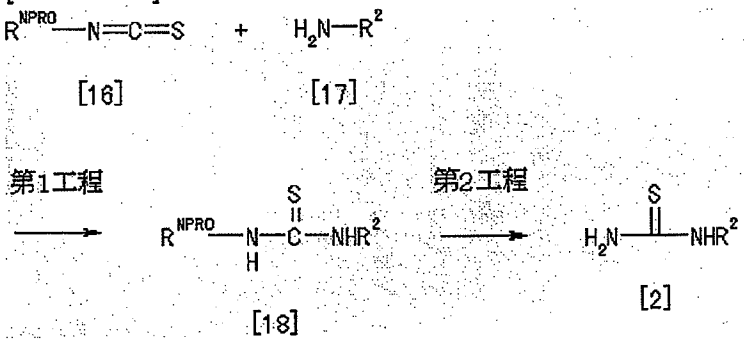
alpha-halo ketone compound [10] can be obtained by making the 2nd process compound [9] react to halogenating agents, such as N-bromosuccinimide, tetrabutylammonium TORIBUROMIDO, a benzyl trimethylammonium dichloroiodate, and bromine, among a solvent and under heating. As a desirable solvent, ether system solvent; methanol, such as dioxane and a tetrahydrofuran, Alcoholic solvent, such as ethanol; Polar-solvent; dichloromethanes, such as dimethyl sulfoxide and acetonitrile, Halogen system solvents, such as chloroform etc.; ester solvent; water or those mixed solvents, such as hydrocarbon system solvent; ethyl acetate, such as benzene and toluene, and butyl acetate, etc. are mentioned.

[0060]A two to two process process is a method of obtaining alpha-halo ketone compound in case Z-Y- is Z-CO-NH-.

[Formula 26]



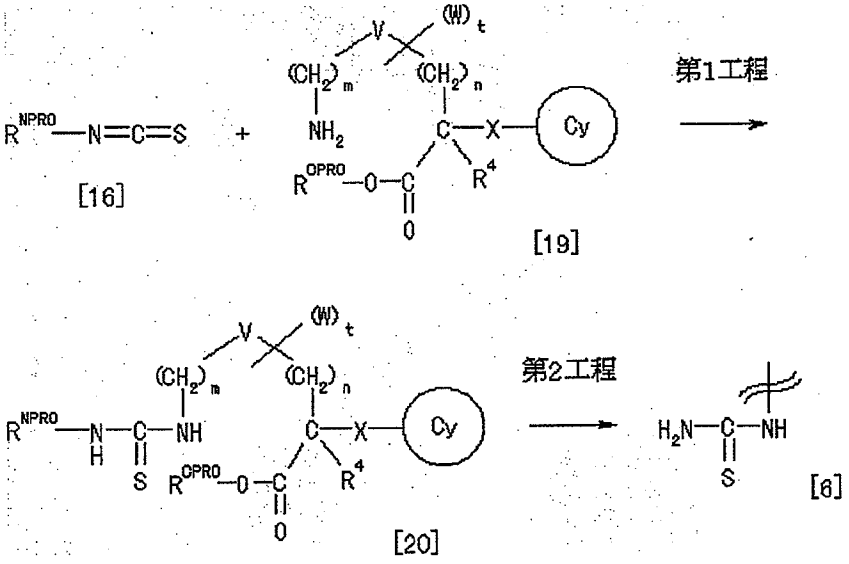
(Each sign is as aforementioned among a formula.)
A compound [12] can be obtained by carrying out ring closure of the diketone compound [8] obtained by a conventional method to thiourea [11] like the 1st process of the 1st process process 2-1.
A compound [14] can be obtained by carrying out amide condensation of a compound [12] and the compound [13] with the 2nd process conventional method.
alpha-halo ketone compound [15] can be obtained from a compound [14] like the 2nd process of the 3rd process process 2-1.
[0061]A three to one process 3 process process is a method of obtaining a thiourea compound as an intermediate of thiazole compound [I].
[Formula 27]



(R^{NPRO} is amine protective groups, such as benzoyl, a tert-butyl group, a tert-butyl carbonyl group, and a tert-butoxycarbonyl group, among a formula, in addition each sign is as aforementioned.)
A compound [18] can be obtained by making an isothiocyanic acid compound [16] obtained by the 1st process conventional method react to an amine compound [17] produced by making it among a solvent be the same as that of a conventional method or the following process 3-2. As a desirable solvent, ether system solvent; methanol, such as dioxane and a tetrahydrofuran, Alcoholic solvent, such as ethanol; Dimethylformamide, dimethyl sulfoxide, Ester solvent [, such as hydrocarbon system solvent; ethyl acetate, such as; benzene and toluene, and butyl acetate], such as halogen system solvents, such as polar-solvent; dichloromethanes, such as acetonitrile and acetone, and chloroform; water or those mixed solvents are mentioned. As for this process, it is preferred to carry out under cooling.
A thiourea compound [2] can be obtained by desorbing a protective group of a compound [18] with the 2nd process conventional method. As an amine protective group, benzoyl, a tert-butyl group, a tert-butyl carbonyl group, a tert-butoxycarbonyl group, etc. are mentioned. For example, what is necessary is just to carry out deprotection in alcoholic solvent, such as methanol and ethanol, using a method of processing by bases, such as potassium carbonate

and sodium hydroxide, when R^{NPRO} is benzoyl.

[0062]Process 3-2 [Formula 28]This process is a method of obtaining a thiourea compound, as an intermediate of a thiazole compound [I'].



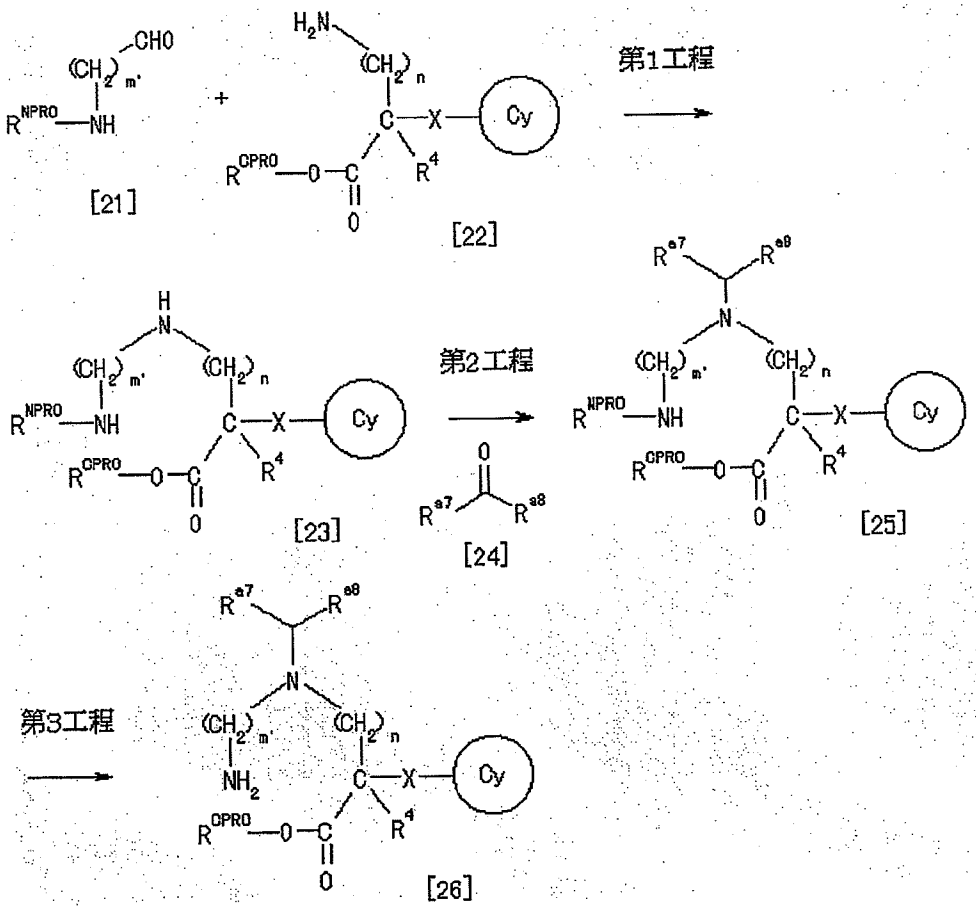
(Passage of the above [the inside of a formula, and each sign].)

A compound [20] can be obtained by making the compound [19] produced by making it be the same as that of the isothiocyanic acid compound [16], the conventional method, or the following process 3-3 acquired with the 1st process conventional method react among solvents, such as methanol and ethanol, and under heating. As a desirable solvent, ether system solvent; methanol, such as dioxane and a tetrahydrofuran, Alcoholic solvent, such as ethanol; Dimethylformamide, dimethyl sulfoxide, Ester solvent [, such as hydrocarbon system solvent; ethyl acetate, such as; benzene and toluene, and butyl acetate], such as halogen system solvents, such as polar-solvent; dichloromethanes, such as acetonitrile and acetone, and chloroform; water or those mixed solvents are mentioned. As for this process, it is preferred to carry out under cooling.

A thiourea compound [6] can be obtained by desorbing an amine protective group of a compound [20] with the 2nd process conventional method. When a compound [19] is an optically active substance, in order to suppress racemization, it is preferred to carry out deprotection under cooling.

[0063]A three to three process process is a method of obtaining a thiazole compound [6] in case V is $-NR^{a5'}-$ in a general formula [I'] and $R^{a5'}$ is a C_{1-6} alkyl group and C_{6-14} aryl C_{1-6} alkyl group, or an intermediate of [19].

[Formula 29]



(m' is 1 or 2 among a formula, and R^{a7} and R^{a8}) Respectively, or it differs, and is C_{1-14} aryl C_{1-6} alkyl groups, such as C_{6-14} aryl group; benzyls, such as C_{1-6} alkyl group; phenyl groups, such as hydrogen atom; methyl, in addition each sign is as aforementioned. Here, $R^{a5'}$ is equivalent to the above-mentioned $-CHR^{a7}R^{a8}$.

A compound [23] can be obtained by making a compound [21] obtained with the 1st process conventional method react to a compound [22] obtained with a conventional method under existence of a reducing agent among a solvent. as a reducing agent -- sodium borohydride, sodium cyanoborohydride, and hydrogenation -- doria -- SETOKISHIHOU -- base -- boron hydride salts, such as sodium, are mentioned. Acid, such as acetic acid and chloride, may be added. As a desirable solvent, ether system solvent; methanol, such as dioxane and a tetrahydrofuran, Alcoholic solvent, such as ethanol; Dimethylformamide, dimethyl sulfoxide, Polar solvents, such as acetonitrile; ester solvent; water or those mixed solvents, such as halogen system solvents, such as dichloromethane and chloroform, etc. are mentioned. [, such as hydrocarbon system solvent; ethyl acetate, such as; benzene and toluene, and butyl

acetate,] Hydrogenation may be performed under existence of catalysts, such as palladium carbon and hydroxylation palladium.
A compound [25] can be obtained by making the 2nd process compound [23] react to a compound [24] obtained with a conventional method under existence of a reducing agent among a solvent. as a reducing agent -- sodium borohydride, sodium cyanoborohydride, and hydrogenation -- doria -- SETOKISHIHOU -- base -- boron hydride salts, such as sodium, are mentioned. Acid, such as acetic acid and chloride, may be added. As a desirable solvent, ether system solvent; methanol, such as dioxane and a tetrahydrofuran, Alcoholic solvent, such as ethanol; Dimethylformamide, dimethyl sulfoxide, Polar solvents, such as acetonitrile; ester solvent; water or those mixed solvents, such as halogen system solvents, such as dichloromethane and chloroform, etc. are mentioned. [, such as hydrocarbon system solvent; ethyl acetate, such as; benzene and toluene, and butyl acetate,] Hydrogenation may be performed under existence of catalysts, such as palladium carbon and hydroxylation palladium. A reaction of the 1st process and the 2nd process can also be performed by replacing an order.
A compound [26] can be obtained by desorbing an amine protective group of a compound [25] with the 3rd process conventional method. As an amine protective group, benzoyl, a tert-butoxycarbonyl group, a benzyloxycarbonyl group, etc. are mentioned. For example, when R^{NPRO} is a tert-butoxycarbonyl group, ; which processes with chloride the bottom of; room temperature which processes with an ethyl acetate solution of chloride among ethyl acetate or methanol solution under a room temperature, and among a tetrahydrofuran -- being certain -- it is -- what is necessary is just to carry out deprotection the bottom of a room temperature, and among methanol using methods, such as processing with chloride-dioxane
[0064]Next, an example explains concretely a compound shown by general formula [I] concerning this invention, and a manufacturing method for the same. However, this invention is not limited by these examples.
[0065]Composition of an example 1N-[4-{2-(cyclo propylcarbonyl amino)-4-methylthiazole 5-yl} thiazole 2-yl]-N-[2-(dimethylamino) ethyl]-2-(2-fluorophenyl) acetamide [0066]3-chloroacetylacetone (237.8mL, 2.085 mol) was added to an ethanol (1000mL) solution of one to process 1 thiourea (151.18 g, 1.986 mol), and it stirred at 90 ** for 1 hour. It is 5-acetyl-2-amino-4-methylthiazole by adding hexane / ethyl acetate (1/1) solution (500mL) after cooling to a room temperature, and ****(ing) a solid which deposited under ice-cooling. A hydrochloride was obtained as white crystals (357.9 g, 94%).
NMR value (six to 300 MHz DMSO-d): 2.43 (s, 3H), 2.51 (s, 3H), 9.32 (br, 1H). [0067]Mix and a 5-acetyl-2-amino-4-methylthiazole hydrochloride (100 g, 519mmol), pyridine (96.5mL, 1194mmol), and chloroform (1000mL) which were obtained at the process 1-1 of one to process 2 Example 1 Under ice-cooling, Cyclopropane carbonylchloride (51.8mL, 571mmol)

was dropped. After stirring for 30 minutes then, it stirred at a room temperature for 2 hours. A reaction mixture was ice-cooled, a solid which deposited by adding water (500mL) was **** (ed), and N-[5-acetyl-4-methylthiazole 2-yl] cyclopropanecarboxamide (112.9 g, 97%) was obtained as white crystals by washing with water (500mL).
NMR value (six to 400 MHz DMSO-d): 0.91-0.96 (m, 4H), 1.9-2.0 (m, 1H), 2.46 (s, 3H), 2.56 (s, 3H). [0068]It is tetrabutylammonium TORIBUROMIDO (255.4 g) to a methanol (500mL) solution of N-[5-acetyl-4-methylthiazole 2-yl] cyclopropanecarboxamide (108.0 g, 482mmol) obtained at the process 1-2 of one to process 3 Example 1. 530mmol was added and it stirred at 85 ** for 2 hours. N-[5-(2-bromoacetyl)-4-methylthiazole 2-yl] cyclopropanecarboxamide was obtained as white crystals (86.3 g, 59%) by ****(ing) a solid which added water (540mL) under ice-cooling, and deposited.
NMR value (six to 400 MHz DMSO-d): 0.91-1.01 (m, 4H), 1.94-2.01 (m, 1H), 2.6 (s, 3H), 4.62 (s, 2H), 12.85 (s, 1H). [0069]mixing process 1-4N,N-dimethylethylenediamine (11.4 g, 129.3mmol) and dioxane (110mL) -- bottom benzoyl isothiocyanic acid of ice-cooling (17.4mL, 129.3mmol) -- in addition, it stirred for 15 minutes as it is. After adding bottom methanol of ice-cooling (55mL), and potassium carbonate (17.9 g, 129.3mmol) to this reaction mixture, it stirred at a room temperature for 2 hours. N-[5-(2-bromoacetyl)-4-methylthiazole 2-yl] cyclopropanecarboxamide (39.2 g, 129.3mmol) obtained at the process 1-3 of Example 1 is added to this reaction mixture under ice-cooling, After stirring at a room temperature for further 1 hour, water was added under ice-cooling, ethyl acetate extracted 4 times, and an organic layer was dried with magnesium sulfate after washing with saturated sodium bicarbonate solution, water, and a saturation salt solution. After filtering magnesium sulfate, By filtering a crystal which added ethyl acetate to residue obtained by carrying out vacuum concentration of the filtrate, and deposited. N-[5-{2-[2-(dimethylamino) ethylamino] thiazole 4-yl}-4-methylthiazole 2-yl] cyclopropanecarboxamide was obtained as a light orange crystal (21.2 g, 47%).
An NMR value. (Six to 300 MHz DMSO-d) :0.88-0.93(m, 4H), 1.87-1.96(m, 1H), 2.18(s, 6H), 2.42-2.47(m, 2H), 2.44(s, 3H), 3.31-3.36(m, 2H), 6.59 (s.) 1H), 7.60(t, 1H, J=6.0Hz), 12.26(s, 1H). [0070]Process 1-52-fluorophenyl acetic acid (110 mg, 0.712mmol), triethylamine (0.107mL, 0.769mmol), and THF (0.5mL) are mixed, Bottom pivaloyl chloride of ice-cooling (0.0879mL, 0.712mmol) was added, and it stirred for 15 minutes at a room temperature. A pyridine solution of N-[5-{2-[2-(dimethylamino) ethylamino] thiazole 4-yl}-4-methylthiazole 2-yl] cyclopropanecarboxamide (100 mg, 0.285mmol) obtained by this reaction mixture at the process 1-4 of Example 1. (2mL) was added and it stirred for 90 minutes at 70 **. After cooling to a room temperature, water and saturated sodium bicarbonate solution were added to a reaction mixture, ethyl acetate extracted, and an organic layer was dried with magnesium sulfate after washing with saturated sodium bicarbonate solution, water, and a saturation salt

solution. Residue obtained by carrying out vacuum concentration of the filtrate is boiled twice with toluene after filtering magnesium sulfate, By filtering a solid which added an ethyl acetate solution of 4-N chloride, and deposited. A title compound N-[4-{2-(cyclo propylcarbonyl amino)-4-methylthiazole 5-yl} thiazole 2-yl]-N-[2-(dimethylamino) ethyl]-2-(2-fluorophenyl) acetamide was obtained as a white solid (81.3 mg, 54%). A chemical constitution formula and a property value of this compound are shown in Table 1.

[0071]Composition of example 2N-[4-methyl-5-{2-(4-methyl-2-oxo 3-phenylpiperazine 1-yl) thiazole 4-yl} thiazole 2-yl]-cyclopropanecarboxamide [0072]process 2-1(R)-(-)-alpha-aminophenyl acetic acid . Methyl ester A hydrochloride (1.15 g, 5.71mmol), a tert-butyl N-(2-oxo ethyl) Cava mate (1.0 g, 6.28mmol), acetic acid (0.425mL, 7.42mmol), and methanol (15mL) are mixed, Bottom sodium cyano borohydride of ice-cooling (431 mg, 6.85mmol) was added, and it stirred as it is for 2 hours. Saturated sodium bicarbonate solution was added to a bottom reaction mixture of ice-cooling, ethyl acetate extracted, and an organic layer was dried with magnesium sulfate after washing with water, saturated sodium bicarbonate solution, and a saturation salt solution. After filtering magnesium sulfate, By refining residue produced by carrying out vacuum concentration of the filtrate with silica gel chromatography (developing solvent: hexane/ethyl acetate =2 / 1 - 1/1). (R)-alpha-[2-(tert-butoxycarbonylamino) ethylamino] phenylacetic acid Methyl ester was obtained as colorless oil (639 mg, 36%).

An NMR value. (Six to 300 MHz DMSO-d) : 1.36(s, 9H), 2.38-2.51(m, 2H), 2.95-3.05(m, 2H), 3.59(s, 3H), 4.39(br, 1H), 6.75(br, 1H), 7.25-7.40(m, 5H.).[0073](R)-alpha-[2-(tert-butoxycarbonylamino) ethylamino] phenylacetic acid methyl ester (3.52 g, 11.42mmol) obtained at the process 2-1 of two to process 2 Example 2, and 37% formalin aqueous solution (3.4 --) [mL and] mixing 45.68mmol, acetic acid (0.719mL, 12.56mmol), and THF (30mL) -- bottom sodium of ice-cooling -- doria -- SETOKISHI borohydride (2.90 g, 13.71mmol) was added, and it stirred as it is for 1 hour. Saturated sodium bicarbonate solution was added to a bottom reaction mixture of ice-cooling, and an organic layer was dried with magnesium sulfate after washing with saturated sodium bicarbonate solution and a saturation salt solution. After filtering magnesium sulfate, By refining residue produced by carrying out vacuum concentration of the filtrate with silica gel chromatography (developing solvent: hexane/ethyl acetate =2/1). (R)-alpha-[N-methyl-N-{2-(tert-butoxycarbonylamino) ethyl} amino] phenylacetic acid Methyl ester was obtained as colorless oil (1.82 g, 50%).

An NMR value. (Six to 400 MHz DMSO-d) : 1.36(s, 9H), 2.19(s, 3H), 2.33-2.50(m,2H), 2.95-3.10(m, 2H), 3.63(s, 3H), 4.37(s, 1H), 6.57(br, 1H), 7.3-7.37(m,5H).[0074](R)-alpha-[N-methyl-N-{2-(tert-butoxycarbonylamino) ethyl} amino] phenylacetic acid obtained at the process 2-2 of two to process 3 Example 2 Methyl ester (1.82 g, 5.66mmol) and ethyl acetate (10mL) are mixed, An ethyl acetate solution (8.5mL, 33.9mmol) of 4-N chloride was added, and it stirred for 2 hours. carrying out azeotropy of the reaction mixture twice with toluene after vacuum

concentration -- (R)-alpha-[N-methyl-N-(2-aminoethyl) amino] phenylacetic acid Methyl ester a rough product of dihydrochloride -- yellow -- it obtained as amorphous. This was used for a next process as it was.

[0075]Process 2-3(R)-alpha-[N-methyl-N-(2-aminoethyl) amino] phenylacetic acid of two to process 4 Example 2 Methyl ester A rough product (5.66mmol) and THF (22mL) of dihydrochloride are mixed, bottom diisopropylethylamine of ice-cooling (2.1mL, 12.4mmol), and benzoyl isothiocyanic acid (0.744mL, 5.66mmol) -- in addition, it stirred for 15 minutes as it is. Water was added to a bottom reaction mixture of ice-cooling, ethyl acetate extracted, and an organic layer was dried with magnesium sulfate after washing with water and a saturation salt solution. carrying out vacuum concentration of the filtrate after filtering magnesium sulfate -- (R)-alpha-[N-methyl-N-{2-(3-benzoylthio ureido) ethyl} amino] phenylacetic acid A rough product of methyl ester was obtained. This was used for a next process as it was.

[0076](R)-alpha-[N-methyl-N-{2-(3-benzoylthio ureido) ethyl} amino] phenylacetic acid obtained at the process 2-4 of two to process 5 Example 2 A rough product (5.66mmol) and methanol (15mL) of methyl ester are mixed, bottom potassium carbonate of ice-cooling (860 mg, 6.22mmol) -- in addition, it stirred as it is for 1 hour. Water was added to a bottom reaction mixture of ice-cooling, ethyl acetate extracted, and an organic layer was dried with magnesium sulfate after washing with a saturation salt solution. It is (R)-alpha-[N-methyl-N-(2-thio ureido ethyl) amino] phenylacetic acid by carrying out vacuum concentration of the filtrate after filtering magnesium sulfate. A rough product of methyl ester was obtained. This was used for a next process as it was.

[0077](R)-alpha-[N-methyl-N-(2-thio ureido ethyl) amino] phenylacetic acid obtained at the process 2-5 of two to process 6 Example 2 A rough product (2.83mmol) and ethanol (6mL) of methyl ester are mixed, N-[5-(2-bromoacetyl)-4-methylthiazole 2-yl] cyclopropanecarboxamide (857 mg, 2.83mmol) obtained at the process 1-3 of Example 1 -- in addition, it flowed back for 5 hours. Saturated sodium bicarbonate solution was added to a bottom reaction mixture of ice-cooling, a mixed solvent of THF and ethyl acetate extracted, and an organic layer was dried with magnesium sulfate. After filtering magnesium sulfate, By filtering a crystal which added methanol to residue produced by carrying out vacuum concentration of the filtrate, and deposited. Title compound N-[4-methyl-5-{2-(4-methyl-2-oxo 3-phenylpiperazine 1-yl) thiazole 4-yl} thiazole 2-yl]-cyclopropanecarboxamide was obtained as white crystals (370 mg, 29%). A chemical constitution formula and a property value of this compound are shown in Table 1.

[0078]Example 3N-[4-methyl-5-{2-(4-methyl-2-oxo 3-phenylpiperazine 1-yl) thiazole 4-yl} thiazole 2-yl]-cyclopropanecarboxamide Composition of a hydrochloride [0079]N-[4-methyl-5-{2- obtained in Example 2. (4-methyl-2-oxo 3-phenylpiperazine 1-yl) To thiazole 4-yl} thiazole 2-yl]-cyclopropanecarboxamide (350 mg, 0.772mmol), ethyl acetate (3.3mL) and an ethyl acetate solution of 4-N chloride. (0.39mL and 1.54mmol) were added and it stirred for 10

minutes. By filtering a depositing solid. A title compound N-[4-methyl-5-{2-(4-methyl-2-oxo 3-phenylpiperazine 1-yl) thiazole 4-yl} thiazole 2-yl]-cyclopropanecarboxamidohydrochloride was obtained as a white solid (390 mg, 100%). A chemical constitution formula and a property value of this compound are shown in Table 1.

Specific optical rotation: [alpha] $_D^{25}$=-116" (c = 0.536, solvent:DMF)

[0080]Composition of an example 4N-[4-methyl-5-{2-(4-methyl-2-oxo 3-phenylpiperazine 1-yl) thiazole 4-yl} thiazole 2-yl]-acetamide [0081]A 5-acetyl-2-amino-4-methylthiazole hydrochloride (100 g, 519mmol), pyridine (96.5mL, 1194mmol), and chloroform (1000mL) which were obtained at the process 1-1 of four to process 1 Example 1 are mixed, Bottom acetylchloride of ice-cooling (40.6mL, 571mmol) was dropped. After stirring then for 1 hour, it stirred at a room temperature for 2 hours. A reaction mixture was ice-cooled, a solid which deposited by adding water (500mL) was ****(ed), and an N-[5-acetyl-4-methylthiazole 2-yl]-acetamide (85.0 g, 77%) was obtained as white crystals by washing with water (500mL).

NMR value (DMSO-d 6-300): 2.17 (s, 3H), 2.47 (s, 3H), 2.56 (s, 3H), 12.43 (s, 1H). [0082]It is tetrabutylammonium TORIBUROMIDO (194.8 g) to a methanol (366mL) solution of an N-[5-acetyl-4-methylthiazole 2-yl]-acetamide (72.8 g, 367mmol) obtained at the process 4-1 of four to process 2 Example 4. 404mmol was added and it stirred at 84 ** for 2 hours. An N-[5-(2-bromoacetyl)-4-methylthiazole 2-yl]-acetamide was obtained as white crystals (63.3 g, 62%) by ****(ing) a solid which added a reaction mixture to water (750mL) under ice-cooling, and deposited.

NMR value (DMSO-d 6-300): 2.18 (s, 3H), 2.58 (s, 3H), 2.65 (s, 2H), 12.57 (s, 1H). [0083](R)-alpha-[N-methyl-N-(2-thio ureido ethyl) amino] phenylacetic acid obtained at the process 2-5 of four to process 3 Example 2 A rough product (2.83mmol) and ethanol (6mL) of methyl ester are mixed, an N-[5-(2-bromoacetyl)-4-methylthiazole 2-yl]-acetamide (857 mg, 2.83mmol) obtained at the process 4-2 of Example 4 -- in addition, it flowed back for 5 hours. Saturated sodium bicarbonate solution was added to a bottom reaction mixture of ice-cooling, a mixed solvent of THF and ethyl acetate extracted, and an organic layer was dried with magnesium sulfate. A rough crystal (517 mg, 43%) was obtained after filtering magnesium sulfate by filtering a crystal which added methanol to residue produced by carrying out vacuum concentration of the filtrate, and deposited. Add ethyl acetate (4mL) to this, and it is made to flow back for 5 minutes, A title compound N-[4-methyl-5-{2-(4-methyl-2-oxo 3-phenylpiperazine 1-yl) thiazole 4-yl} thiazole 2-yl]-acetamide was obtained as white crystals (355 mg, 30%) by filtering an after-cooling crystal to a room temperature. A chemical constitution formula and a property value of this compound are shown in Table 1.

[0084]Example 5N-[4-methyl-5-{2-(4-methyl-2-oxo 3-phenylpiperazine 1-yl) thiazole 4-yl} thiazole 2-yl]-acetamide Composition of a hydrochloride [0085]An ethyl acetate solution (0.4mL, 1.6mmol) of ethyl acetate (50mL) and 4-N chloride was added for having obtained in

Example 4 (340 mg, 0.795mmol), and it stirred for 10 minutes. It is a title compound N-[4-methyl-5-{2-(4-methyl-2-oxo 3-phenylpiperazine 1-yl) thiazole 4-yl} thiazole 2-yl]-acetamide by filtering a depositing solid. A hydrochloride was obtained as a white solid (374 mg, 100%). A chemical constitution formula and a property value of this compound are shown in Table 2.

Specific optical rotation: $[\alpha]_D^{25}$=-116" (c = 0.541, solvent:DMF)

[0086]A compound of Examples 6-306 was obtained from Example 6 like example 306 Examples 1-5. A chemical constitution formula and a property value of this compound are shown in Table 77 from Table 2.

[0087]

[Table 1]

[0088]

[Table 2]

表 1

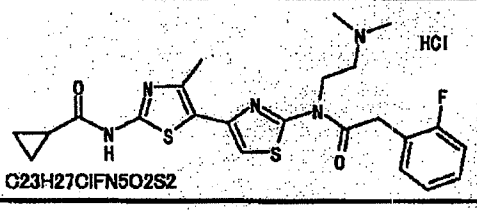
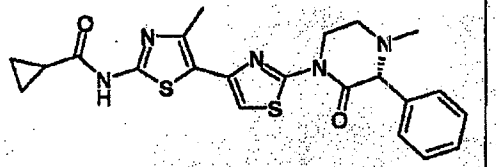
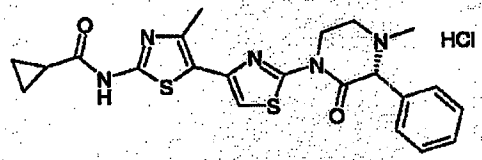
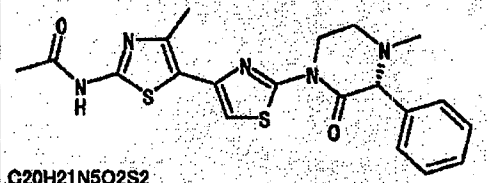
実施例番号	構造式 / 組成式	純度(%) / 性状 / 融点(℃)	1H NMR(δ)ppm	MS
1	 C23H27ClFN5O2S2	>90 結晶 >220	DMSO-d6-300 0.71-0.98(m, 4H), 1.90-1.99(m, 1H), 2.51(s, 3H), 2.96(s, 3H), 2.97(s, 3H), 3.57(br, 2H), 4.29(s, 2H), 4.71(br, 2H), 7.2-7.27(m, 2H), 7.34(s, 2H), 7.36-7.45(m, 2H), 10.49(br, 1H), 12.41(s, 2H)	ESI+ 488(100)
2	 C22H23N5O2S2	142-156	DMSO-d6-400 0.89-0.94(m, 4H), 1.92-1.99(m, 1H), 2.14(s, 3H), 2.48(s, 3H), 2.84(dt, 1H, J=3.40, 11.8Hz), 3.24-3.30(m, 1H), 4.1(s, 1H), 4.11(dt, 1H, J=4.4, 12.1Hz), 4.43(d, 1H, J=15.7Hz), 7.29(s, 1H), 7.32-7.41(m, 5H), 12.34(s, 1H)	ESI+ 454(100)
3	 C22H24ClN5O2S2	>90 アモルファス	DMSO-d6-300 0.86-0.94(m, 4H), 1.91-1.99(m, 1H), 2.50(s, 3H), 2.58(s, 3H), 3.6(br, 2H), 4.59(br, 2H), 7.41(s, 1H), 7.47-7.6(m, 5H), 12.42(s, 1H)	ESI+ 454(100)
4	 C20H21N5O2S2	211-214	DMSO-d6-400 2.13(s, 3H), 2.14(s, 3H), 2.48(s, 3H), 2.85(dt, 1H, J=3.40, 11.8Hz), 3.24-3.39(m, 1H), 4.1(s, 1H), 4.08-4.16(m, 1H), 4.44(dt, 1H, J=11.8, 2.94Hz), 7.31(s, 1H), 7.32-7.41(m, 5H), 12.05(s, 1H)	ESI+ 428(100)

表 2

実施例番号	構造式／組成式	純度（%）／性状／融点（℃）	1H NMR(δ)ppm	MS
5	C20H22ClN5O2S2	>90 結晶 >220	DMSO-d6-300 2.16(s, 3H), 2.50(s, 3H), 2.67(s, 3H), 3.71-3.99(m, 2H), 4.65(br, 2H), 5.52(br, 1H), 7.43(s, 1H), 7.46-7.70(m, 5H), 12.12(s, 1H)	ESI+ 428(10)
6	C17H16N4O2S2	>90 結晶 >200	DMSO-d6-300 2.13(s, 3H), 2.46(s, 3H), 3.78(s, 2H), 7.20(s, 1H), 7.24-7.35(m, 5H), 12.06(brs, 1H), 12.52(brs, 1H)	ESI+ 373(100)
7	C18H18N4O3S2	>90 結晶 198 - 200	DMSO-d6-300 1.25(t, 3H, J=6.9Hz), 2.43(s, 3H), 3.78(s, 2H), 4.20(q, 2H, J=6.9Hz), 7.18(s, 1H), 7.24-7.35(m, 5H), 11.63(brs, 1H), 12.51(brs, 1H)	ESI+ 403(100)
8	C19H18N4O3S2	>90 結晶 >230	DMSO-d6-300 2.13(s, 3H), 2.47(s, 3H), 3.75(s, 3H), 3.77(s, 2H), 6.91(t, 1H, J=7.32Hz), 6.98(d, 1H, J=8.07Hz), 7.18(s, 1H), 7.22(d, 1H, J=7.32Hz), 7.26(t, 1H, J=8.07Hz), 12.09(s, 1H), 12.82(s, 1H)	ESI+ 403(100)

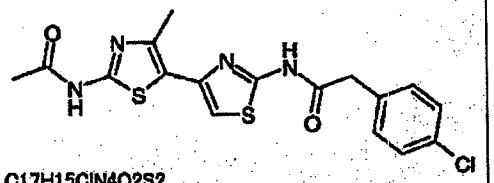
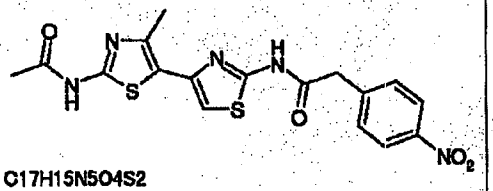
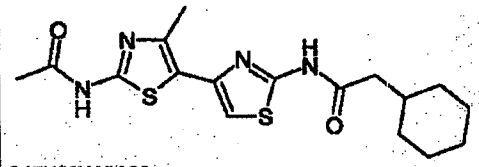
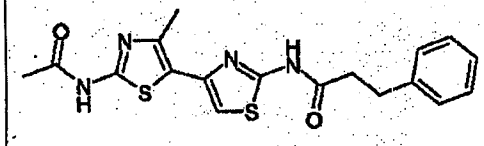
[0089]

[Table 3]

[0090]

[Table 4]

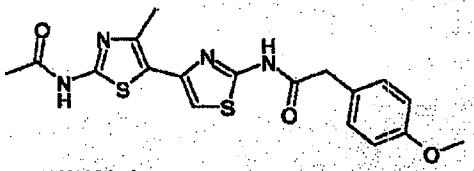
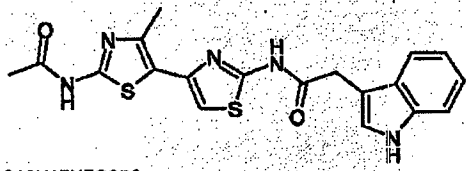
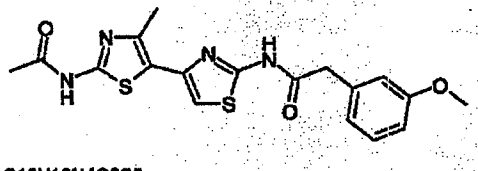
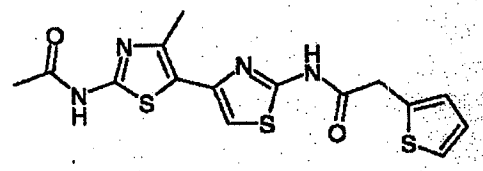
表 3

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
9	 C17H15ClN4O2S2	>90 結晶 >230	DMSO-d6-300 2.13(s, 3H), 2.46(s, 3H), 3.80(s, 2H), 7.20(s, 1H), 7.39(dd, 4H, J=8.4, 14.6Hz), 12.08(s, 1H)	ESI+ 407(100)
10	 C17H15N5O4S2	>90 結晶 >230	DMSO-d6-300 2.13(s, 3H), 2.46(s, 3H), 3.98(s, 2H), 7.22(s, 1H), 7.62(d, 2H, J=8.79Hz), 8.22(d, 2H, J=8.79Hz), 12.06(s, 1H), 12.62(s, 1H)	ESI+ 418(100)
11	 C17H22N4O2S2	>90 結晶 224-224.9 dec.	DMSO-d6-300 0.81-1.31(m, 5H), 1.61-1.85(m, 6H), 2.13(s, 3H), 2.33(d, 2H, J=7.4Hz), 2.46(s, 3H), 7.17(s, 1H), 12.07(s, 1H), 12.23(s, 1H)	ESI+ 379(100)
12	 C18H18N4O2S2	>90 結晶 212.7 - 213.9	DMSO-d6-300 2.13(s, 3H), 2.46(s, 3H), 2.77(t, 2H, J=7.4Hz), 2.94(t, 2H, J=7.4Hz), 7.2(s, 1H), 7.2-7.33(m, 5H), 12.06(s, 1H), 12.29(s, 1H)	ESI+ 387(100)

[0091]

[Table 5]

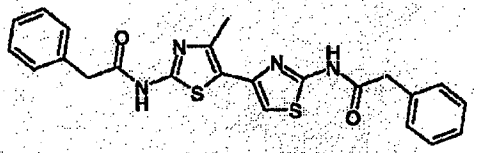
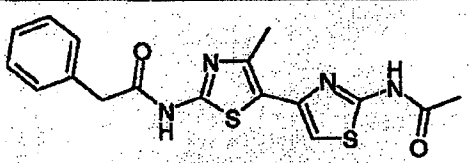
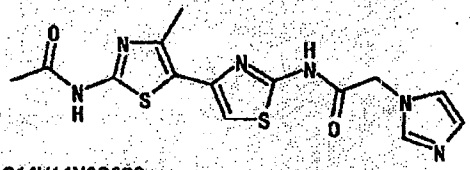
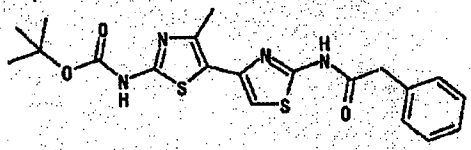
表 4

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
13	 C18H18N4O3S2	>90 結晶 >230	DMSO-d6-300 2.13(s, 3H), 2.46(s, 3H), 3.69(s, 2H), 3.73(s, 3H), 6.89(d, 2H, J=8.79Hz), 7.19(s, 1H), 7.25(d, 2H, J=8.79Hz), 12.05(s, 1H), 12.46(s, 1H)	ESI+ 403(100)
14	 C19H17N5O2S2	>90 結晶 >230	DMSO-d6-300 1.99(s, 3H), 2.46(s, 3H), 3.88(s, 2H), 7.01(t, 1H, J=6.8Hz), 7.09(t, 1H, J=6.8Hz), 7.3(d, 1H, J=2.2Hz), 7.37(d, 1H, J=8.1Hz), 7.6(d, 1H, J=8.1Hz), 10.97(s, 1H), 12.07(s, 1H), 12.48(s, 1H)	ESI+ 412(100)
15	 C18H18N4O3S2	>90 結晶 >230	DMSO-d6-300 2.14(s, 3H), 2.46(s, 3H), 3.75(s, 3H), 3.75(s, 2H), 6.85(d, 1H, J=7.9Hz), 6.92(d, 1H, J=7.9Hz), 6.93(s, 1H), 7.21(s, 1H), 7.26(t, 1H, J=7.9Hz), 12.08(s, 1H), 12.52(s, 1H)	ESI+ 403(100)
16	 C15H14N4O2S3	>90 結晶 >230	DMSO-d6-300 2.14(s, 3H), 2.47(s, 3H), 4.03(s, 2H), 6.99-7.04(m, 2H), 7.23(s, 1H), 7.43(dd, 1H, J=1.5, 4.8Hz), 12.08(s, 1H), 12.57(s, 1H)	ESI+ 379(100)

[0092]

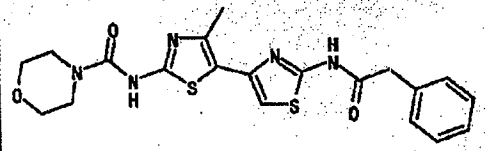
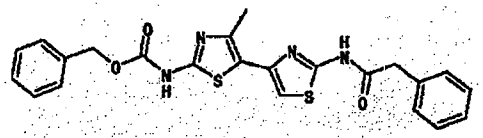
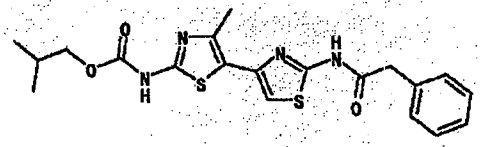
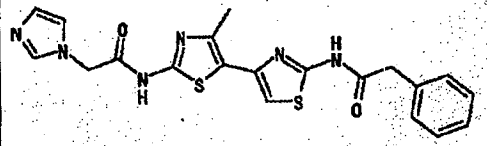
[Table 6]

表 5

実施例番号	構造式 / 組成式	純度 (%) / 性状 / 融点 (℃)	1H NMR(δ)ppm	MS
17	 C23H20N4O2S2	>90 結晶 210.2 - 210.7	DMSO-d6-300 2.47(s, 3H), 3.76(s, 2H), 3.78(s, 2H), 7.19(s, 1H), 7.19-7.39(m, 10H), 12.32(s, 1H), 12.51(s, 1H)	ESI+ 449(100)
18	 C17H16N4O2S2	>90 結晶 133.5 - 136.5	DMSO-d6-300 2.15(s, 3H), 2.47(s, 3H), 3.76(s, 2H), 7.18(s, 1H), 7.19-7.39(m, 5H), 12.24(s, 1H), 12.32(s, 1H)	ESI+ 373(100)
19	 C14H14N6O2S2	>90 結晶 >250	DMSO-d6-400 2.14(s, 3H), 2.47(s, 3H), 5.04(s, 2H), 6.90(s, 1H), 7.18(s, 1H), 7.23(s, 1H), 7.64(s, 1H), 12.06(brs, 1H), 12.70(brs, 1H)	ESI+ 363(100)
20	 C20H22N4O3S2	>90 アモルファス	CDCl3-300 1.54(s, 9H), 2.48(s, 3H), 3.84(s, 2H), 6.84(s, 1H), 7.29-7.46(m, 5H), 8.84(brs, 1H)	ESI- 429(100)

[0093]
[Table 7]

表 6

実施例番号	構造式 ／ 組成式	純度（%）／性状／融点（℃）	1H NMR(δ)ppm	MS
21	 C20H21N5O3S2	>90 アモルファス	DMSO-d6-300 2.48(s, 3H), 3.49(brs, 4H), 3.57(brd, 4H, J=4.4Hz), 3.77(s, 2H), 7.11(s, 1H), 7.26-7.34(m, 5H), 10.85(brs, 1H), 12.48(brs, 1H)	ESI+ 444(100)
22	 C23H20N4O3S2	>90 アモルファス	DMSO-d6-300 2.42(s, 3H), 3.78(s, 2H), 5.22(s, 2H), 7.18(s, 1H), 7.26-7.42(m, 10H), 11.78(brs, 1H), 12.50(brs, 1H)	ESI+ 465(100)
23	 C20H22N4O3S2	>90 結晶 212 - 214	DMSO-d6-400 0.92(d, 6H, J=6.7Hz), 1.93(m, 1H), 2.43(s, 3H), 3.78(s, 2H), 3.94(d, 2H, J=6.7Hz), 7.17(s, 1H), 7.25-7.34(m, 5H), 11.63(brs, 1H), 12.49(brs, 1H)	ESI+ 431(100)
24	 C20H18N6O2S2	>90 結晶 >250	DMSO-d6-300 2.46(s, 3H), 3.76(s, 2H), 5.99(s, 2H), 6.89(s, 1H), 7.17(s, 1H), 7.19(s, 1H), 7.24-7.33(m, 5H), 7.63(s, 1H), 12.48(brs, 1H)	ESI+ 439(100)

[0094]

[Table 8]

表 7

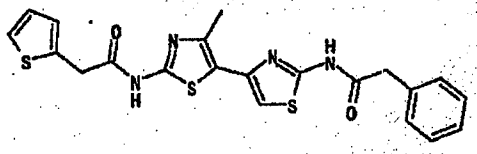
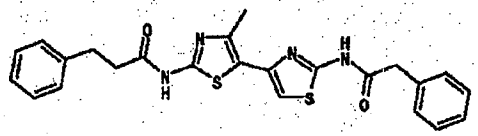
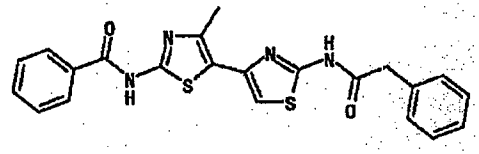
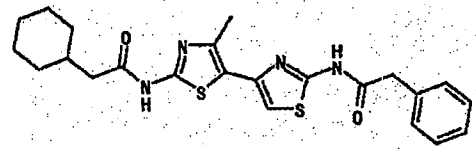
実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
25	 C21H18N4O2S3	>90 結晶 201 - 203	DMSO-d6-300 2.46(s, 3H), 3.77(s, 2H), 3.98(s, 2H), 6.97(m, 1H), 6.98(s, 1H), 7.20(s, 1H), 7.25-7.41(m, 5H), 7.41(d, 1H, J=1.4Hz), 12.34(brs, 1H), 12.51(brs, 1H)	ESI+ 455(100)
26	 C24H22N4O2S2	>90 アモルファス	CDCl3-300 2.45(s, 3H), 2.71(t, 2H, J=7.7Hz), 3.05(t, 2H, J=7.7Hz), 3.84(s, 2H), 6.87(s, 1H), 7.17-7.45(m, 10H), 8.82(brs, 1H)	ESI+ 463(100)
27	 C22H18N4O2S2	>90 結晶 229 - 231	DMSO-d6-300 0.90-0.98(m, 2H), 1.13-1.23(m, 2H), 1.61-1.66(m, 6H) ,1.77(m, 1H), 2.29(brd, 2H, J=7.4Hz), 2.45(s, 3H), 3.78(s, 2H), 7.18(s, 1H), 7.25-7.34(m, 5H), 12.00(brs, 1H), 12.50(brs, 1H)	ESI+ 455(100)
28	 C23H26N4O2S2	>90 アモルファス	DMSO-d6, 300MH 0.90-0.98(m, 2H), 1.13-1.23(m, 2H), 1.61-1.66(m, 6H) ,1.77(m, 1H), 2.29(brd, 2H, J=7.4Hz), 2.45(s, 3H), 3.78(s, 2H), 7.18(s, 1H), 7.25-7.34(m, 5H), 12.00(brs, 1H), 12.50(brs, 1H)	ESI+ 455(100)

表 8

実施例番号	構造式 / 組成式	純度 (%) / 性状 / 融点 (℃)	1H NMR(δ)ppm	MS
29	C18H18N4O2S2	>90 アモルファス	DMSO-d6-400 1.45(d, 3H, J=7.1Hz), 2.12(s, 3H), 2.44(s, 3H), 4.01(q, 1H, J=7.1Hz), 7.19(s, 1H), 7.24-7.39(m, 5H), 12.03(s, 1H), 12.43(s, 1H)	ESI+ 387(100)
30	C18H18N4O3S2	>90 結晶 217.1 - 218.6	DMSO-d6-300 2.13(s, 3H), 2.45(s, 3H), 3.34(s, 3H), 5.05(s, 1H), 7.23(s, 1H), 7.34-7.52(m, 5H), 12.06(s, 1H), 12.54(s, 1H)	ESI+ 403(100)
31	C17H15N5O4S2	>80 結晶 >220	DMSO-d6-300 2.13(s, 3H), 2.46(s, 3H), 3.99(s, 2H), 7.22(s, 1H), 7.65(t, 1H, J=7.87Hz), 7.8(d, 1H, J=7.87Hz), 8.15(d, 1H, J=8.87Hz), 8.26(s, 1H), 12.06(s, 1H), 12.61(s, 1H)	ESI+ 418(100)
32	C17H15FN4O2S2	>90 結晶 >220	DMSO-d6-300 2.14(s, 3H), 2.46(s, 3H), 3.79(s, 2H), 7.16(d, 1H, J=8.8Hz), 7.19(d, 1H, J=8.8Hz), 7.21(s, 1H), 7.37(d, 1H, J=8.8Hz), 7.39(d, 1H, J=8.8Hz), 12.08(s, 1H), 12.51(s, 1H)	ESI+ 391(100)

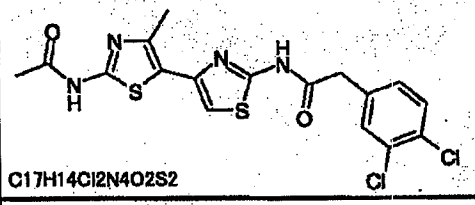
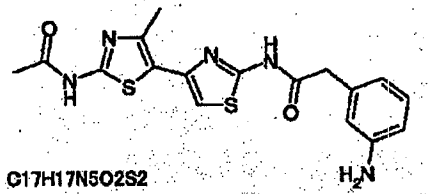
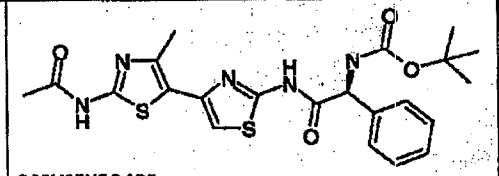
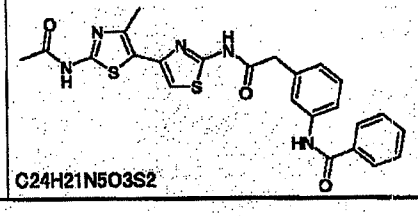
[0095]

[Table 9]

[0096]

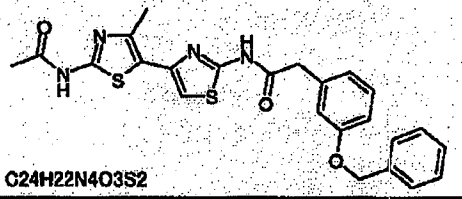
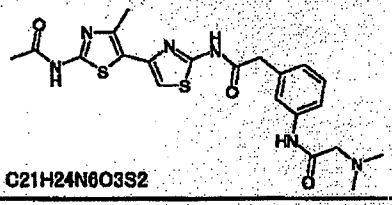
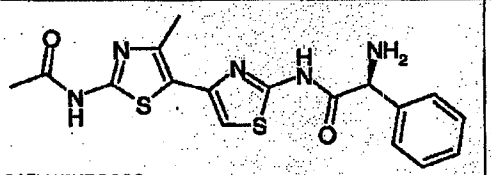
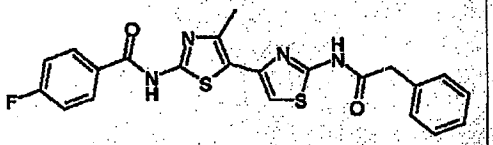
[Table 10]

表 9

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
33	 C17H14Cl2N4O2S2	>90 結晶 >220	DMSO-d6-300 2.14(s, 3H), 2.47(s, 3H), 3.84(s, 2H), 7.35(d, 1H, J=8.3Hz), 7.35(d, 1H, J=8.3Hz), 7.62(d, 1H, J=8.3Hz), 7.63(s, 1H), 12.08(s, 1H), 12.56(s, 1H)	ESI+ 441(100)
34	 C17H17N5O2S2	>90 結晶 >220	DMSO-d6-300 2.14(s, 3H), 2.46(s, 3H), 3.59(s, 2H), 5.05(s, 2H), 6.45(d, 1H, J=7.3Hz), 6.47(d, 1H, J=7.3Hz), 6.53(s, 1H), 6.96(t, 1H, J=7.3Hz), 7.20(s, 1H), 12.08(s, 1H), 12.46(s, 1H)	ESI+ 388(100)
35	 C22H25N5O4S2	>90 結晶 >220	DMSO-d6-400 1.39(s, 9H), 2.12(s, 3H), 2.45(s, 3H), 5.46(br, 1H), 7.21(s, 1H), 7.31(s, 3H), 7.49(d, 2H, J=6.7Hz), 7.69(br, 1H), 12.04(s, 1H), 12.57(s, 1H)	ESI+ 488(82)
36	 C24H21N5O3S2	>90 結晶 >220	DMSO-d6-300 2.14(s, 3H), 2.47(s, 3H), 3.8(s, 2H), 7.1(d, 1H, J=7.3Hz), 7.22(s, 1H), 7.33(t, 1H, J=7.9Hz), 7.51-7.62(m, 3H), 7.7(d, 1H, J=9.2Hz), 7.8(s, 1H), 7.97(d, 2H, J=6.6Hz), 10.28(s, 2H), 12.08(s, 2H), 12.58(s, 2H)	ESI+ 492(100)

[0097]
[Table 11]

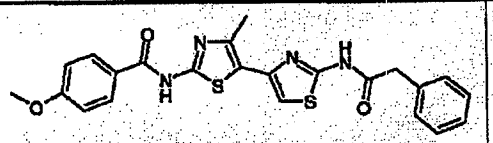
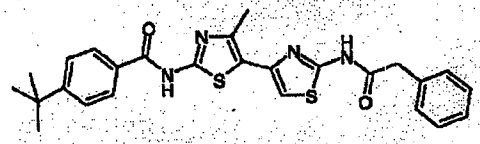
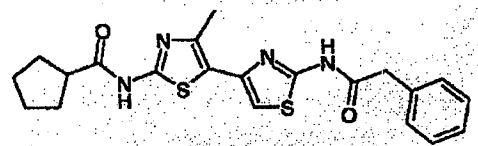
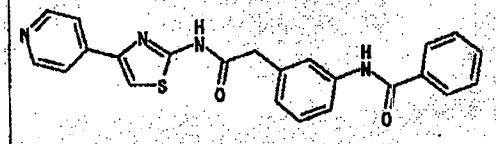
表 10

実施例番号	構造式 ／ 組成式	純度 ／性状／ 融点 (%) (℃)	1H NMR(δ)ppm	MS
37	 C24H22N4O3S2	>90 結晶 >220	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.75(s, 2H), 5.09(s, 2H), 6.92(d, 2H, J=7.7Hz), 7.02(br, 1H), 7.2(s, 1H), 7.25(t, 1H, J=7.9Hz), 7.32(d, 1H, J=7.1Hz), 7.38(d, 2H, J=14.8Hz), 7.45(d, 2H, J=7.1Hz), 12.04(s, 1H), 12.48(s, 1H)	ESI+ 479(100)
38	 C21H24N6O3S2	>90 アモルファス	DMSO-d6-300 2.14(s, 3H), 2.28(s, 6H), 2.47(s, 3H), 3.06(s, 2H), 3.75(s, 2H), 7.04(d, 1H, J=7.9Hz), 7.21(s, 1H), 7.27(t, 1H, J=7.9Hz), 7.56(d, 1H, J=7.9Hz), 7.66(s, 1H), 9.72(s, 1H), 12.08(s, 1H), 12.55(s, 1H)	ESI+ 473(100)
39	 C17H17N5O2S2	>90 結晶 >220	DMSO-d6-300 2.12(s, 3H), 2.44(s, 3H), 4.62(s, 1H), 7.06(s, 1H), 7.21-7.37(m, 3H), 7.46(d, 2H, J=7.32Hz)	ESI+ 388(100)
40	 C22H17FN4O2S2	>90 結晶 197.1 - 199	DMSO-d6-400 2.52(s, 3H), 3.8(s, 2H), 7.25-7.4(m, 8H), 8.16-8.2(m, 2H), 12.53(s, 1H), 12.63(s, 1H)	ESI+ 453(100)

[0098]

[Table 12]

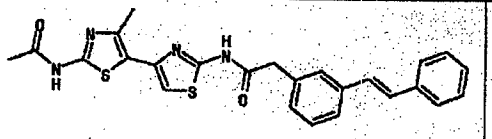
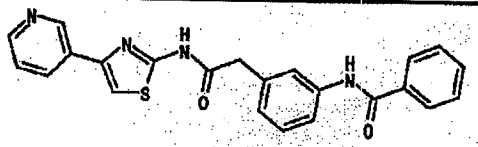
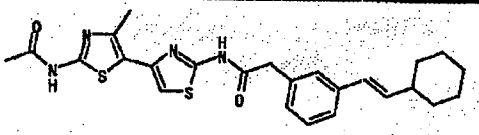
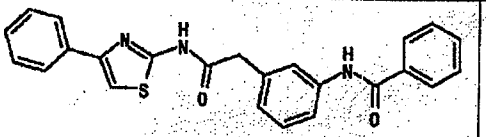
表 11

実施例番号	構造式 / 組成式	純度(%) / 性状 / 融点(℃)	1H NMR(δ)ppm	MS
41	 C23H20N4O3S2	>90 結晶 230.2 - 232.2	DMSO-d6-400 2.52(s, 3H), 3.8(s, 2H), 3.85(s, 3H), 7.07(d, 2H, J=8.72Hz), 7.23-7.35(m, 6H), 8.1(d, 2H, J=8.84Hz)	ESI+ 465(100)
42	 C26H26N4O2S2	>90 結晶 192.4 - 195.3	DMSO-d6-400 1.32(s, 9H), 2.52(s, 3H), 3.8(s, 2H), 7.18-7.35(m, 6H), 7.56(d, 2H, J=8.48Hz), 8.05(d, 2H, J=8.44Hz), 12.53(br, 2H)	ESI+ 491(100)
43	 C21H22N4O2S2	>90 結晶 115.8 - 118.9	DMSO-d6-400 1.55-1.89(m, 8H), 2.46(s, 3H), 2.88-2.92(m, 1H), 3.79(s, 2H), 7.16-7.34(m, 6H), 12.01(s, 1H), 12.5(s, 1H)	ESI+ 427(100)
44	 C23H18N4O2S	>90 結晶 248 - 250	DMSO-d6-300 3.82(s, 2H), 7.10(d, 1H, J=7.7Hz), 7.32(d, 1H, J=7.7Hz), 7.50-7.59(m, 3H), 7.68(d, 1H, J=9.2Hz), 7.80-7.85(m, 3H), 7.94-7.98(m, 3H), 8.61-8.63(m, 2H), 10.26(brs, 1H), 12.63(brs, 1H)	ESI+ 415(100)

[0099]

[Table 13]

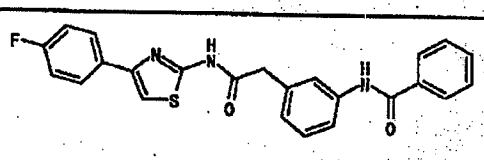
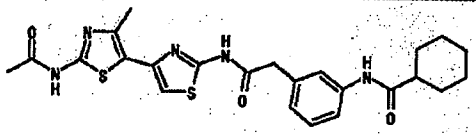
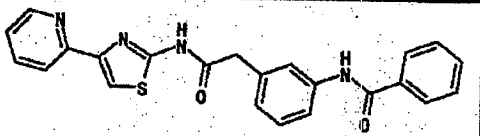
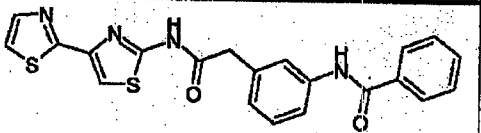
表 12

実施例番号	構造式 / 組成式	純度(%) / 性状 / 融点(℃)	1H NMR(δ)ppm	MS
45	 C25H22N4O2S2	>90 結晶 >250	DMSO-d6-400 1.15-1.31(m, 5H), 1.65-1.80(m, 5H), 2.13(s, 3H), 2.13(m, 1H), 2.46(s, 3H), 3.76(s, 2H), 6.23(dd, 1H, J=6.6, 16.0Hz), 6.35(d, 1H, J=16.0Hz), 7.17(m, 1H), 7.19(s, 1H), 7.24-7.27(m, 2H), 7.35(m, 1H), 12.03(brs, 1H), 12.48(brs, 1H)	ESI+ 481(100)
46	 C23H18N4O2S	>90 結晶 >250	DMSO-d6-400 3.81(s, 2H), 7.10(d, 1H, J=7.7Hz), 7.32(t, 1H, J=7.7Hz), 7.46(dd, 1H, J=5.1, 8.2Hz), 7.50-7.59(m, 3H), 7.68(d, 1H, J=9.2Hz), 7.79(s,1H), 7.80(s,1H), 7.94-7.96(m, 2H), 8.22(dt, 1H, J=2.0, 6.1Hz), 8.52(dd, 1H, J=1.5, 4.7Hz), 9.11(d, 1H, J=2.0Hz), 10.25(brs,	ESI+ 415(100)
47	 C25H26N4O2S2	>90 結晶 >250	DMSO-d6, 400MH 1.15-1.31(m, 5H), 1.65-1.80(m, 5H), 2.13(s, 3H), 2.13(m, 1H), 2.46(s, 3H), 3.76(s, 2H), 6.23(dd, 1H, J=6.6, 16.0Hz), 6.35(d, 1H, J=16.0Hz), 7.17(m, 1H), 7.19(s, 1H), 7.24-7.27(m, 2H), 7.35(m, 1H), 12.03(brs, 1H), 12.48(brs, 1H)	ESI+ 481(100)
48	 C24H19N3O2S	>90 結晶 216.6 - 218.2	DMSO-d6-300 3.77(s, 2H), 7.05-7.67(m, 9H), 7.77(s, 1H), 7.86-7.93(m, 4H), 10.5(s, 1H), 12.5(s, 1H)	ESI+ 414(100)

[0100]

[Table 14]

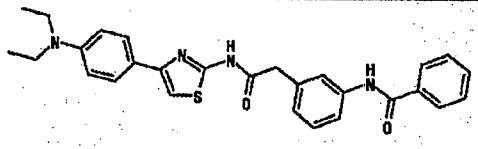
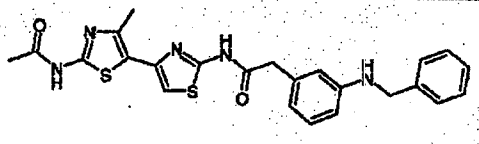
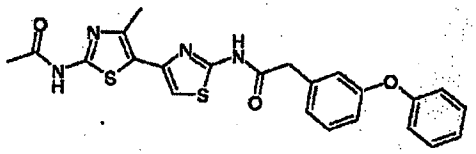
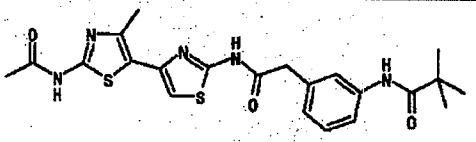
表 13

実施例番号	構造式 / 組成式	純度 (%) / 性状 / 融点 (℃)	1H NMR(δ)ppm	MS
49	 C24H18FN3O2S	>90 結晶 232.6 - 233.2	DMSO-d6-300 3.8(s, 3H), 7.09(d, 1H, J=7.71Hz), 7.24-7.34(m, 3H), 7.5-7.59(m, 4H), 7.71(d, 1H, J=7.71Hz), 7.8(s, 1H), 7.91-7.98(m, 4H), 10.25(s, 1H), 12.51(s, 1H)	ESI+ 432(100)
50	 C24H27N5O3S2	>90 結晶 225.2 - 227.2	DMSO-d6-300 1.22-1.41(m, 5H), 1.65-1.8(m, 5H), 2.13(s, 3H), 2.28(br, 1H), 2.46(s, 3H), 3.73(s, 2H), 6.99(d, 1H, J=5.67Hz), 7.19(s, 1H), 7.23(t, 1H, J=5.91Hz), 7.49(d, 1H, J=6.27Hz), 7.61(s, 1H), 9.77(s, 1H), 12.04(s, 1H), 12.51(s, 1H)	ESI+ 498(100)
51	 C23H18N4O2S	>90 結晶 212 - 214	DMSO-d6-400 3.81(s, 2H), 7.10(d, 1H, J=7.6Hz), 7.30-7.34(m, 2H), 7.50-7.59(m, 3H), 7.69(d, 1H, J=7.9Hz), 7.80(s, 1H), 7.81(s, 1H), 7.87-7.96(m, 3H), 8.59(d, 1H, J=4.5Hz), 10.25(brs, 1H), 12.55(brs, 1H)	ESI+ 415(100)
52	 C21H16N4O2S2	>90 結晶 223 - 225	DMSO-d6-400 3.81(s, 2H), 7.09(d, 1H, J=7.6Hz), 7.32(t, 1H, J=7.6Hz), 7.50-7.59(m, 3H), 7.68(d, 1H, J=7.9Hz), 7.74-7.76(m, 2H), 7.80(s, 1H), 7.88(d, 1H, J=3.3Hz), 7.95(d, 2H, J=7.1Hz), 10.25(brs, 1H), 12.72(brs, 1H)	ESI+ 421(100)

[0101]

[Table 15]

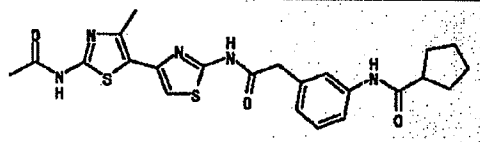
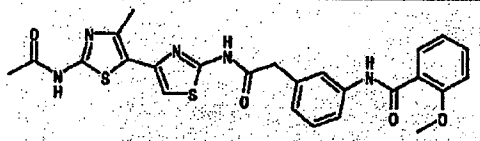
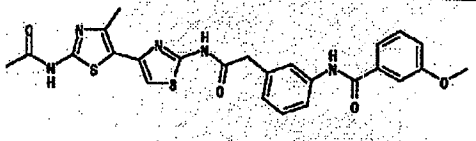
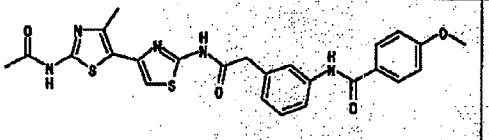
表 14

実施例番号	構造式 / 組成式	純度(%) / 性状 / 融点(℃)	1H NMR(δ)ppm	MS
53	 C28H28N4O2S	>90 結晶 214 - 216	DMSO-d6-400 1.10(t, 6H, J=7.0Hz), 3.36(q, 4H, J=7.0Hz), 3.78(s, 2H), 6.68(d, 2H, J=8.9Hz), 7.09(d, 1H, J=7.8Hz), 7.29(s, 1H), 7.31(t, 1H, J=7.6Hz), 7.50-7.60(m, 3H), 7.67(d, 2H, J=8.9Hz), 7.94(s, 1H), 7.95(d, 2H, J=7.0Hz), 10.24(brs, 1H), 12.41(brs, 1H)	ESI+ 485(100)
54	 C24H23N5O2S2	>90 アモルファス	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.6(s, 2H), 4.24(d, 2H, J=5.85Hz), 6.24(t, 1H, J=5.85Hz), 6.43(d, 1H, J=8.2Hz), 6.49(d, 1H, J=7.6Hz), 6.6(s, 1H), 6.97(t, 1H, J=7.9Hz), 7.17-7.31(m, 4H), 7.35(d, 2H, J=7.1Hz), 12.03(s, 1H), 12.42(s, 1H)	ESI+ 478(100)
55	 C23H20N4O3S2	>90 結晶 164.4 - 166.8	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.77(s, 2H), 6.99(t, 4H, J=8.1Hz), 7.13(t, 1H, J=7.4Hz), 7.2(s, 1H), 7.34-7.4(m, 4H), 12.04(s, 1H), 12.5(s, 1H)	ESI+ 465(100)
56	 C22H25N5O3S2	>90 結晶 230	DMSO-d6-400 1.22(s, 9H), 2.13(s, 3H), 2.46(s, 3H), 3.79(s, 2H), 7.02(d, 1H, J=7.52Hz), 7.19(s, 1H), 7.24(t, 1H, J=7.86Hz), 7.54(d, 1H, J=8.2Hz), 7.63(s, 1H), 9.18(s, 1H), 12.04(s, 1H), 12.51(s, 1H)	ESI+ 472(100)

[0102]

[Table 16]

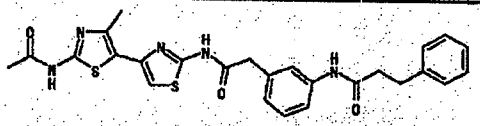
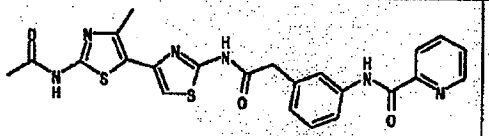
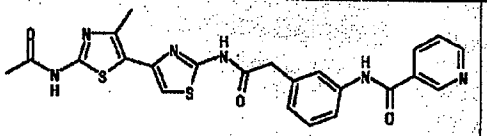
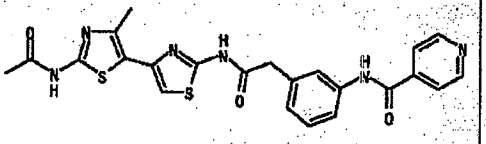
表 15

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
57	 C23H25N5O3S2	>90 結晶 230	DMSO-d6-400 1.54-1.84(m, 8H), 2.13(s, 3H), 2.46(s, 3H), 2.74-2.78(m, 1H), 3.74(s, 2H), 6.99(d, 1H, J=7.44Hz), 7.2(s, 1H), 7.23(t, 1H, J=7.82Hz), 7.5(d, 1H, J=8.16Hz), 7.6(s, 1H), 9.83(s, 1H), 12.04(s, 1H), 12.51(s, 1H)	ESI+ 484(100)
58	 C25H23N5O4S2	>90 結晶 230	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.78(s, 2H), 3.89(s, 3H), 7.06-7.08(m, 2H), 7.16-7.19(m, 2H), 7.29(t, 1H, J=8Hz), 7.49-7.61(m, 3H), 7.77(s, 1H), 10.1(s, 1H), 11.9(s, 1H), 12.58(s, 1H)	ESI+ 522(100)
59	 C25H23N5O4S2	>90 結晶 153.6 - 156.5	DMSO-d6-400 2.13(s, 3H), 2.49(s, 3H), 3.79(s, 2H), 3.84(s, 3H), 7.08-7.10(m, 2H), 7.20(s, 1H), 7.30-7.55(m, 4H), 7.67-7.69(m, 1H), 7.77(s, 1H), 10.2(s, 1H), 12.0(s, 1H), 12.54(s, 1H)	ESI+ 522(100)
60	 C25H23N5O4S2	>90 結晶 219.8 - 222	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.78(s, 2H), 3.84(s, 3H), 7.04-7.07(m, 3H), 7.20(s, 1H), 7.27-7.32(m, 1H), 7.66-7.68(m, 1H), 7.77(s, 1H), 7.95-7.97(m, 2H), 10.08(s, 1H), 12.03(s, 1H), 12.53(s, 1H)	ESI+ 522(100)

[0103]

[Table 17]

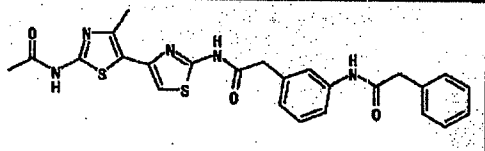
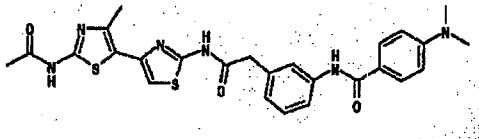
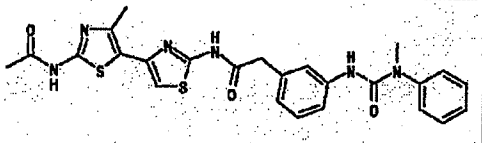
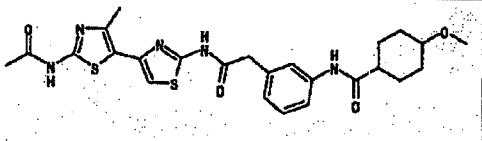
表 16

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
61	 C26H25N5O3S2	>90 結晶 193 - 195.6	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 2.61(t, 2H, J=7.7Hz), 2.9(t, 2H, J=7.68Hz), 3.74(s, 2H), 7(d, 1H, J=7.64Hz), 7.15-7.29(m, 7H), 7.48-7.55(m, 2H), 9.88(s, 1H), 12.03(s, 1H), 12.51(s, 1H)	ESI+ 520(100)
62	 C23H20N6O3S2	>90 結晶 230	DMSO-d6-400 2.13(s, 3H), 2.49(s, 3H), 3.8(s, 2H), 7.11(d, 1H, J=7.52Hz), 7.2(s, 1H), 7.33(dd, 1H, J=7.88, 7.84Hz), 7.66-7.69(m, 1H), 7.75-7.77(m, 1H), 7.79(s, 1H), 8.05-8.07(m, 1H), 8.16(d, 1H, J=7.76Hz), 8.73-8.74(m, 1H), 10.59(s, 1H), 12.03(s, 1H), 12.54(s, 1H)	ESI+ 493(100)
63	 C23H20N6O3S2	>90 結晶 230	DMSO-d6-400 2.11(s, 3H), 2.49(s, 3H), 3.67(s, 2H), 6.95(br, 1H), 7.09(d, 1H, J=7.64Hz), 7.29(dd, 1H, J=7.84, 7.72Hz), 7.54-7.57(m, 1H), 7.67-7.71(m, 2H), 8.29(d, 1H, J=8.04Hz), 8.74-8.75(m, 1H), 9.1-9.1(m, 1H), 9.1-9.1(m, 1H), 10.42(s, 1H), 12.15(br, 1H)	ESI+ 493(100)
64	 C23H20N6O3S2	>90 結晶 230	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.8(s, 2H), 7.13(d, 1H, J=7.56Hz), 7.2(s, 1H), 7.34(dd, 1H, J=7.88, 7.84Hz), 7.69(d, 1H, J=8.08Hz), 7.77(s, 1H), 7.86(d, 1H, J=5.84Hz), 8.78(d, 1H, J=5.84Hz), 10.49(s, 1H), 12.03(s, 1H), 12.54(s, 1H)	ESI+ 493(100)

[0104]

[Table 18]

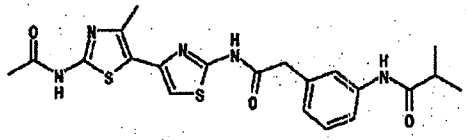
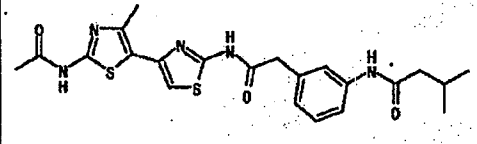
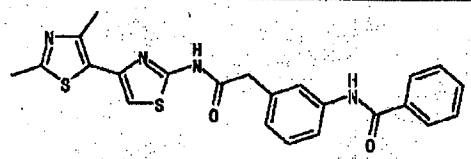
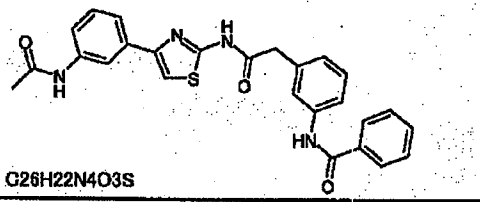
表 17

実施例番号	構造式 ／ 組成式	純度（%）／性状／ 融点（℃）	1H NMR(δ)ppm	MS
65	 C25H23N5O3S2	>90 結晶 210.3 - 212.2	DMSO-d6-400 2.13(s, 3H), 2.49(s, 3H), 3.62(s, 2H), 3.74(s, 2H), 7.01(d, 1H, J=7.64Hz), 7.19-7.33(m, 7H), 7.51(d, 1H, J=8.04Hz), 7.57(s, 2H), 10.13(s, 1H), 12.03(s, 1H), 12.5(s, 1H)	ESI+ 506(100)
66	 C26H26N6O3S2	>90 結晶 230	DMSO-d6-400 2.11(s, 3H), 2.44(s, 3H), 2.99(s, 6H), 2.99(s, 6H), 3.64(s, 2H), 6.75(d, 2H, J=9Hz), 7.01(d, 2H, J=7.56Hz), 7.23(dd, 1H, J=7.92, 7.92Hz), 7.66-7.7(m, 2H), 7.87(d, 2H, J=8.88Hz), 9.82(s, 1H), 12.15(br, 1H)	ESI+ 535(100)
67	 C25H24N6O3S2	>90 結晶 230	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.26(s, 3H), 3.7(s, 3H), 6.93(d, 2H, J=7.68Hz), 7.15-7.42(m, 9H), 8.11(s, 1H), 12.03(s, 1H), 12.47(s, 1H)	ESI+ 521(100)
68	 C25H29N5O4S2	>90 結晶 204.3 - 206.5	DMSO-d6-400 1.05-1.19(m, 1H), 1.39-1.6(m, 3H), 1.69-1.95(m, 3H), 2.02-2.1(m, 1H), 2.13(s, 3H), 2.25-2.39(m, 1H), 2.46(s, 3H), 3.21(s, 3Hx1/2), 3.24(s, 3Hx1/2), 3.73(s, 2H), 6.99(d, 1H, J=7.12Hz), 7.19-7.25(m, 2H), 7.46-7.52(m, 1H), 7.59(s, 1H), 9.77(s, 1Hx1/2), 9.82(	ESI+ 528(100)

[0105]

[Table 19]

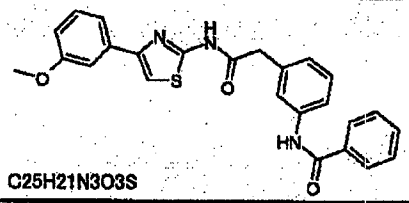
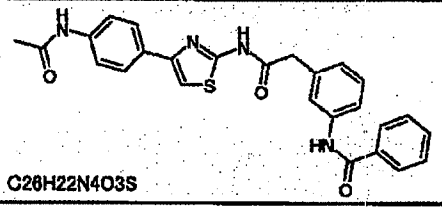
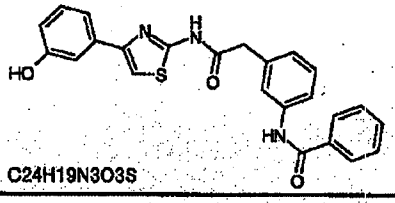
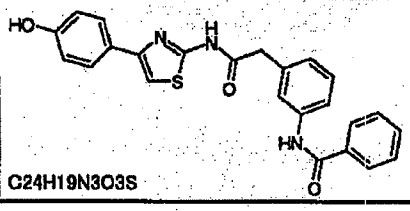
表 18

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
69	 C21H23N5O3S2	>90 結晶 >230	DMSO-d6-300 1.08(s, 3H), 1.1(s, 3H), 2.13(s, 3H), 2.46(s, 3H), 2.51-2.6(m, 1H), 3.74(br, 2H), 7(d, 1H, J=7.68Hz), 7.2(s, 1H), 7.24(dd, 1H, J=7.68, 7.68Hz), 7.51(d, 1H, J=8.04Hz), 7.6(s, 1H), 9.82(s, 1H), 12.06(s, 1H), 12.54(s, 1H)	ESI+ 458(100)
70	 C22H25N5O3S2	>90 結晶 >230	DMSO-d6-300 0.91(s, 3H), 0.93(s, 3H), 2.05-2.1(m, 1H), 2.13(s, 3H), 2.16(s, 2H), 3.74(s, 2H), 7(d, 1H, J=7.68Hz), 7.2(s, 1H), 7.24(dd, 1H, J=8.07, 7.68Hz), 7.5(d, 1H, J=8.43Hz), 7.58(s, 1H), 9.84(s, 1H), 12.05(s, 1H), 12.53(s, 1H)	ESI+ 472(100)
71	 C23H20N4O2S2	>90 結晶 218 - 220	DMSO-d6-400 2.50(s, 3H), 2.59(s, 3H), 3.79(s, 2H), 7.08(d, 1H, J=7.5Hz), 7.27(s, 1H), 7.31(t, 1H, J=7.1Hz), 7.59(m, 1H), 7.67(d, 1H, J=8.2Hz), 7.79(s, 1H), 7.95(d, 2H, J=7.1Hz), 10.24(brs, 1H), 12.57(brs, 1H)	ESI+ 449(100)
72	 C26H22N4O3S	>90 結晶 >220	DMSO-d6-400 2.06(s, 3H), 3.81(s, 2H), 7.1(d, 1H, J=7.6Hz), 7.31-7.61(m, 8H), 7.69(d, 1H, J=8.1Hz), 7.8(s, 1H), 7.96(d, 2H, J=7.1Hz), 8.23(s, 2H), 9.96(s, 1H), 10.25(s, 1H), 12.53(s, 1H)	ESI+ 471(100)

[0106]

[Table 20]

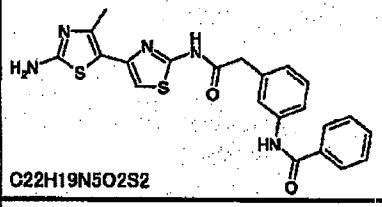
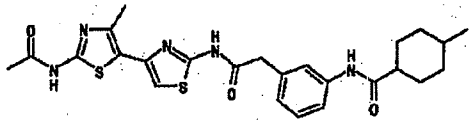
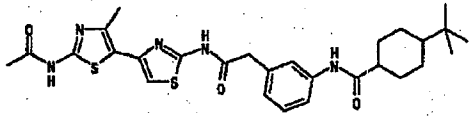
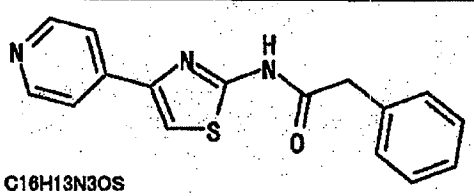
表 19

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
73	 C25H21N3O3S	>90 結晶 190.8 - 191.8	DMSO-d6-400 3.8(s, 3H), 6.89(dd, 1H, J=3.1, 8.2Hz), 7.1(d, 1H, J=7.6Hz), 7.33(dd, 2H, J=7.6, 15.2Hz), 7.46-7.69(m, 7H), 7.8(s, 1H), 7.96(d, 2H, J=7.1Hz), 10.24(s, 1H), 12.51(s, 1H)	ESI+ 444(100)
74	 C26H22N4O3S	>90 結晶 >220	DMSO-d6-400 2.06(s, 3H), 3.8(s, 2H), 7.11(d, 1H, J=8.1Hz), 7.33(t, 1H, J=7.65Hz), 7.48(s, 1H), 7.51-7.71(m, 7H), 7.81(s, 1H), 7.82(d, 2H, J=8.7Hz), 7.97(d, 2H, J=7.1Hz), 9.98(s, 1H), 10.24(s, 1H), 12.49(s, 1H)	ESI+ 471(100)
75	 C24H19N3O3S	>90 結晶 129 - 132.1	DMSO-d6-300 3.80(s, 2H), 6.73(d, 1H, J=6.93Hz), 7.1(d, 1H, J=7.35Hz), 7.21(t, 1H, J=7.7Hz), 7.28-7.34(m, 3H), 7.49-7.61(m, 4H), 7.69(d, 1H, J=8.07Hz), 7.80(s, 1H), 7.95(d, 2H, J=8.43Hz), 9.47(s, 1H), 10.27(s, 1H), 12.51(s, 1H)	ESI+ 430(100)
76	 C24H19N3O3S	>90 結晶 >220	DMSO-d6-300 3.79(s, 2H), 6.81(d, 2H, J=11.3Hz), 7.1(d, 1H, J=8.1Hz), 7.31(d, 1H, J=8.1Hz), 7.35(s, 1H), 7.49-7.73(m, 6H), 7.81(s, 1H), 7.96(d, 2H, J=8.1Hz), 9.56(s, 1H), 10.27(s, 1H), 12.47(s, 1H)	ESI+ 430(100)

[0107]

[Table 21]

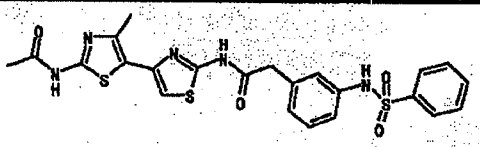
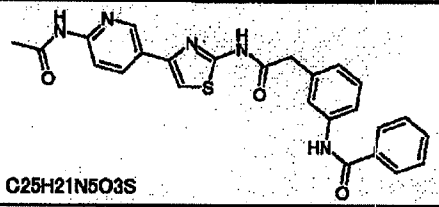
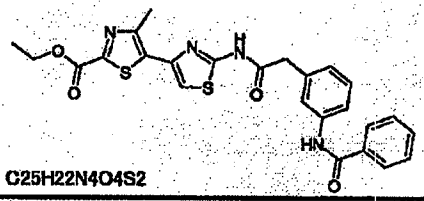
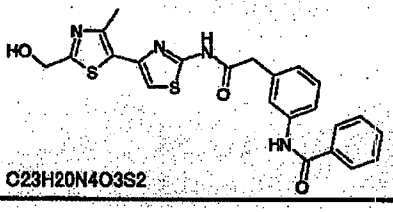
表 20

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
77	 C22H19N5O2S2	>90 結晶 >220	DMSO-d6-400 2.29(s, 3H), 3.78(s, 2H), 6.92(s, 1H), 6.93(d, 2H, J=5.1Hz), 7.08(d, 1H, J=7.2Hz), 7.31(t, 1H, J=7.9Hz), 7.51-7.61(m, 3H), 7.68(d, 1H, J=7.9Hz), 7.78(s, 1H), 7.96(d, 2H, J=7.1Hz), 10.24(s, 1H), 12.43(s, 1H)	ESI+ 450(100)
78	 C25H29N5O3S2	>90 結晶 223 - 224.5	DMSO-d6-400 0.88(d, 3Hx1/2, J=6.52Hz), 0.93(d, 3Hx1/2, J=6.96Hz), 1.4-1.59(m, 5H), 1.78-1.84(m, 3H), 2.13(s, 3H), 2.46(s, 3H), 3.73(s, 2H), 6.99(d, 2H, J=7.6Hz), 7.16-7.25(m, 2H), 7.48(d, 1H, J=7.84Hz), 7.17(s, 2H), 9.76(s, 1Hx1/2), 9.82(s, 1Hx1/2), 12.07(s, 1H), 12.	ESI+ 512(100)
79	 C28H35N5O3S2	>90 結晶 183.3 - 186.9	DMSO-d6-400 0.81(s, 9Hx1/2), 0.84(d, 9Hx1/2), 1.0(br, 2H), 1.3-1.59(m, 4H), 1.76-1.92(m, 2H), 2.04-2.11(m, 1H), 2.13(s, 3H), 2.19-2.28(m, 1H), 2.46(s, 3H), 3.73(s, 2H), 6.99(d, 1H, J=7.68Hz), 7.21-7.25(m, 2H), 7.48(d, 1H, J=8.16Hz), 7.61(s, 1H), 9.68(s, 1Hx1/2), 9.8(	ESI+ 554(100)
80	 C16H13N3OS	>90 結晶 >220	DMSO-d6-400 3.81(s, 2H), 7.26-7.35(m, 5H), 7.83(d, 2H, J=3.04Hz), 7.98(s, 1H), 8.62(d, 2H, J=3Hz), 12.62(s, 1H)	ESI+ 296(100)

[0108]

[Table 22]

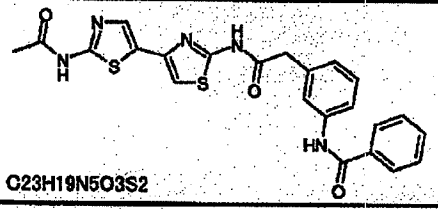
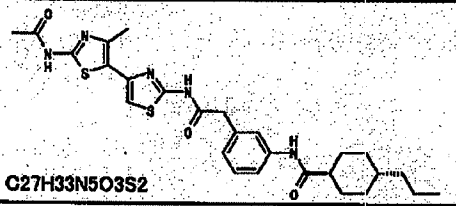
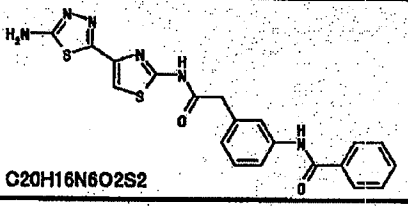
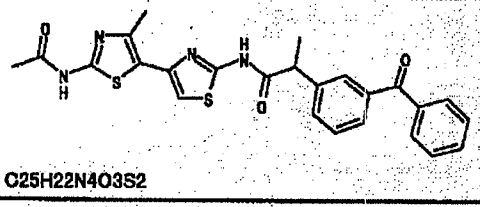
表 21

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
81	 C23H21N5O4S3	>90 結晶 >220 dec.	DMSO-d6-400 2.13(s, 3H), 2.47(s, 3H), 3.68(s, 2H), 6.93-7(m, 2H), 7.11-7.21(m, 3H), 7.4-7.58(m, 4H), 7.71-7.77(m, 2H), 10.27(s, 1H), 12.04(s, 1H), 12.48(s, 1H)	ESI+ 528(100)
82	 C25H21N5O3S	>90 結晶 >220	DMSO-d6-300 2.11(s, 3H), 3.81(s, 2H), 7.11(d, 1H, J=7.3Hz), 7.33(t, 1H, J=7.85Hz), 7.51-7.71(m, 5H), 7.82(s, 1H), 7.97(d, 2H, J=8.8Hz), 8.15(d, 1H, J=8.8Hz), 8.23(dd, 1H, J=2.2, 8.8Hz), 8.85(d, 1H, J=2.2Hz), 10.28(s, 1H), 10.6(s, 1H), 12.61(s, 1H)	ESI+ 472(100)
83	 C25H22N4O4S2	>90 結晶 >220	DMSO-d6-400 1.34(t, 3H, J=7.1Hz), 2.65(s, 3H), 3.82(s, 2H), 4.37(q, 2H, J=7.1Hz), 7.09(d, 1H, J=7.7Hz), 7.32(t, 1H, J=7.9Hz), 7.51-7.61(m, 4H), 7.68(d, 1H, J=7.9Hz), 7.8(s, 1H), 7.96(d, 2H, J=7.1Hz), 10.25(s, 1H), 12.66(s, 1H)	ESI+ 507(100)
84	 C23H20N4O3S2	>90 アモルファス	DMSO-d6-300 3.81(s, 2H), 4.68(d, 1H, J=5.7Hz), 6.01(t, 1H, J=5.7Hz), 7.1(d, 1H, J=7.6Hz), 7.32(d, 1H, J=8.1Hz), 7.34(d, 1H, J=8.1Hz), 7.52-7.63(m, 3H), 7.69(d, 1H, J=8.1Hz), 7.81(s, 1H), 7.97(d, 2H, J=8.1Hz), 10.28(s, 1H), 12.61(s, 1H)	ESI+ 465(100)

[0109]

[Table 23]

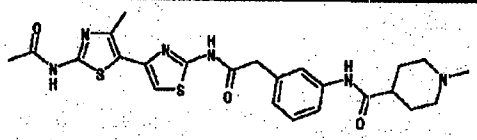
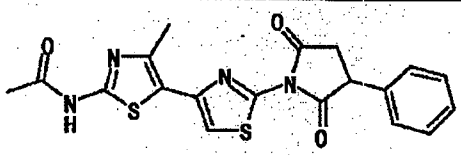
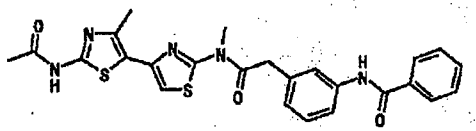
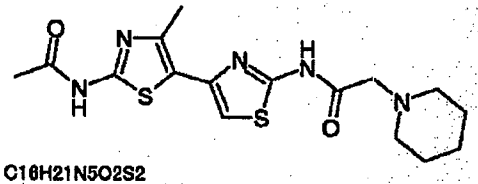
表 22

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
85	 C23H19N5O3S2	>90 結晶 >220	DMSO-d6-400 2.15(s, 3H), 3.79(s, 2H), 7.09(d, 1H, J=7.6Hz), 7.31(t, 1H, J=7.85Hz), 7.42(s, 1H), 7.51-7.61(m, 3H), 7.69(d, 1H, J=8.1Hz), 7.79(s, 1H), 7.81(s, 1H), 7.96(d, 2H, J=7.1Hz), 10.24(s, 1H), 12.11(s, 1H), 12.58(s, 1H)	ESI+ 478(100)
86	 C27H33N5O3S2	>90 結晶 230 - 232	DMSO-d6-400 0.86(t, 3H, J=7.4Hz), 0.86-0.93(m, 2H), 1.14-1.43(m, 7H), 1.79(brt, 4H, J=13.2Hz), 2.13(s, 3H), 2.27(m, 1H), 2.46(s, 3H), 3.73(s, 2H), 6.98(d, 1H, J=7.8Hz), 7.19(s, 1H), 7.23(t, 1H, J=7.8Hz), 7.48(d, 1H, J=7.8Hz), 7.61(brs, 1H), 9.78(brs, 1H), 12.03(brs,	ESI+ 540(100)
87	 C20H16N6O2S2	>90 結晶 >250	DMSO-d6-300 3.78(s, 2H), 7.07(d, 1H, J=7.3Hz), 7.27-7.33(m, 3H), 7.48-7.58(m, 3H), 7.64(s, 1H), 7.67(d, 1H, J=8.1Hz), 7.78(s, 1H), 7.94(dd, 2H, J=1.1, 7.7Hz), 10.25(brs, 1H), 12.65(brs, 1H)	ESI+ 437(100)
88	 C25H22N4O3S2	>90 結晶 139.5 - 141.7	DMSO-d6-300 1.49(d, 3H, J=6.96Hz), 2.12(s, 3H), 2.45(s, 3H), 4.1-4.15(m, 1H), 7.21(s, 1H), 7.53-7.75(m, 8H), 7.81(s, 1H), 12.05(s, 1H), 12.53(s, 1H)	ESI+ 491(100)

[0110]

[Table 24]

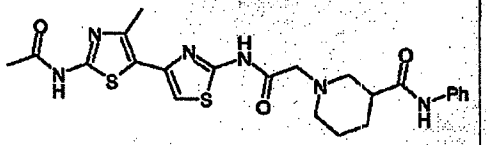
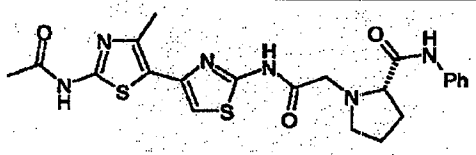
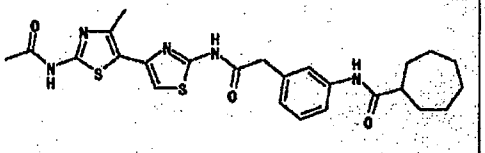
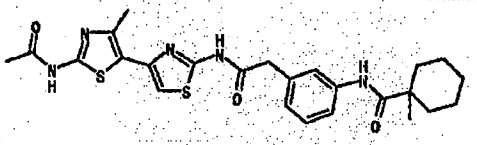
表 23

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
89	 C24H28N6O3S2	>90 結晶 >220	DMSO-d6-300 1.61-1.92(m, 4H), 2.01-2.13(m, 5H), 2.27-2.39(m, 4H), 2.91-2.99(m, 2H), 3.74(s, 2H), 7(d, 1H, J=7.47Hz), 7.2-7.31(m, 2H), 7.48(d, 1H, J=8.1Hz), 7.61(s, 1H), 9.89(s, 1H), 12.02(br, 1H), 12.54(s, 1H)	ESI+ 513(100)
90	 C19H16N4O3S2	>90 アモルファス	CDCl3-300 2.27(s, 3H), 2.62(s, 3H), 3.13(dd, 1H, J=5.5, 18.7Hz), 3.47(dd, 1H, J=9.9, 18.7Hz), 4.29(dd, 1H, J=5.5, 9.9Hz), 7.25(s, 1H), 7.33-7.46(m, 5H)	ESI+ 413(100)
91	 C25H23N5O3S2	>90 結晶 >250	DMSO-d6-400 2.14(s, 3H), 2.48(s, 3H), 3.78(s, 3H), 4.15(s, 2H), 7.04(d, 1H, J=7.5Hz), 7.26(s, 1H), 7.33(t, 1H, J=7.1Hz), 7.50-7.60(m, 3H), 7.70(m, 1H), 7.72(s, 1H), 7.95(d, 2H, J=7.1Hz), 10.25(brs, 1H), 12.03(brs, 1H)	ESI+ 506(100)
92	 C16H21N5O2S2	>90 結晶 193.8 - 194.9	DMSO-d6-400 1.38(br, 2H), 1.52(br, 4H), 2.13(s, 3H), 2.46(s, 3H), 3.26(br, 4H), 12.03(s, 1H)	ESI+ 380(100)

[0111]

[Table 25]

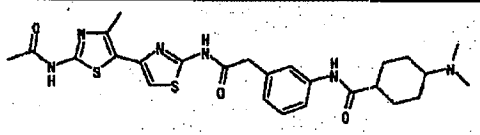
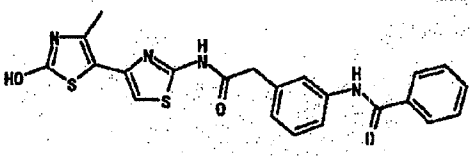
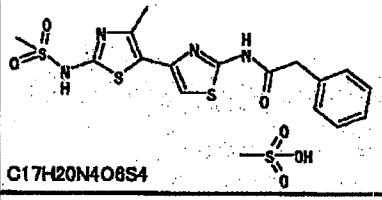
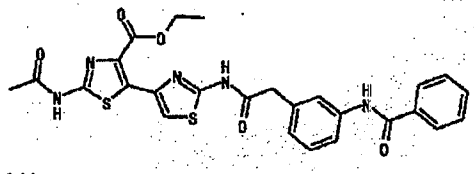
表 24

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
93	 C23H26N6O3S2	>90 結晶 >220	DMSO-d6-400 1.5-1.83(m, 3H), 2.13(s, 3H), 2.31-2.38(m, 1H), 2.58-2.88(m, 3H), 3.36(dd, 2H, J=15.7, 21.8Hz), 7.02(t, 1H, J=7.4Hz), 7.22(s, 1H), 7.28(t, 2H, J=7.4Hz), 7.63(d, 2H, J=7.4Hz), 10.04(s, 1H), 12.04(s, 1H), 12.11(s, 1H)	ESI+ 499(100)
94	 C22H24N6O3S2	>90 アモルファス	DMSO-d6-400 1.75-1.95(m, 3H), 2.18-2.24(m, 1H), 2.62-2.68(m, 1H), 3.21-3.26(m, 1H), 3.44-3.49(m, 1H), 3.59(d, 1H, J=16.3Hz), 3.8(d, 1H, J=16.3Hz), 7.06(t, 1H, J=7.35Hz), 7.23(s, 1H), 7.32(t, 2H, J=7.85Hz), 7.68(d, 2H, J=7.7Hz), 10.16(s, 1H), 12.05(s, 1H), 12.32(s, 1H	ESI+ 485(100)
95	 C25H29N5O3S2	>90 結晶 >220	DMSO-d6-300 1.34-1.85(m, 13H), 2.13(s, 3H), 2.46(s, 3H), 3.73(s, 2H), 6.99(d, 1H, J=7.38Hz), 7.2-7.31(m, 2H), 7.47(d, 2H, J=7.95Hz), 7.6(s, 1H), 9.78(s, 1H), 12.06(s, 1H), 12.54(s, 1H)	ESI+ 512(100)
96	 C25H29N5O3S2	>90 結晶 >220	DMSO-d6-400 1.17(s, 3H), 1.25-1.68(m, 8H), 2.05-2.09(m, 2H), 2.13(s, 3H), 2.46(s, 3H), 3.74(s, 2H), 7.02(d, 1H, J=7.76Hz), 7.2-7.26(m, 2H), 7.54(d, 1H, J=8.36Hz), 7.63(s, 1H), 9.16(s, 1H), 12.04(s, 1H), 12.51(s, 1H)	ESI+ 512(100)

[0112]

[Table 26]

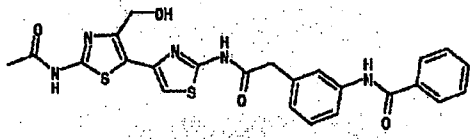
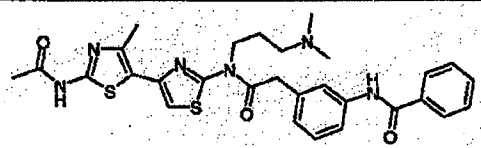
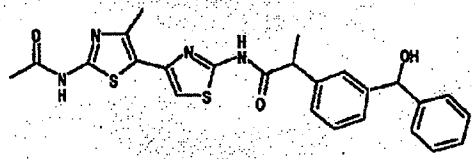
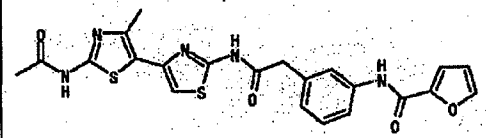
表 25

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
97	 C26H32N6O3S2	>90 結晶 199.7 - 201.3	DMSO-d6-400 1.52(br, 4H), 1.81(br, 2H), 1.91(br, 2H), 2.13(s, 3H), 2.3(br, 6H), 2.46(s, 3H), 3.74(s, 2H), 7(d, 1H, J=7.4Hz), 7.2-7.25(m, 2H), 7.48(d, 2H, J=8Hz), 7.59(s, 1H), 9.76(s, 1H), 12.04(s, 1H), 12.51(s, 1H)	ESI+ 541(100)
98	 C22H18N4O3S2	>90 結晶 177-179 dec.	DMSO-d6-300 2.27(s, 3H), 3.78(s, 2H), 7.06-7.08(m, 2H), 7.29-7.33(m, 1H), 7.5-7.6(m, 5H), 7.78(s, 1H), 7.95(d, 2H, J=6.96Hz), 10.26(s, 1H), 11.28(s, 1H), 12.54(s, 1H)	ESI+ 451(100)
99	 C17H20N4O6S4	>90 結晶 184 - 186	DMSO-d6-300 2.58(s, 3H), 3.11(s, 3H), 3.77(s, 2H), 3.88(s, 3H), 7.24-7.33(m, 5H), 7.45(s, 1H), 12.62(brs, 1H)	ESI+ 409(100)
100	 C26H23N5O5S2	>90 結晶 165 - 167	DMSO-d6-300 2.12(s, 3H), 3.77(s, 2H), 4.56(d, 2H, J=5.5Hz), 5.21(t, 1H, J=5.5Hz), 7.08(d, 1H, J=7.7Hz), 7.30(t, 1H, J=7.7Hz), 7.35(s, 1H), 7.50-7.57(m, 3H), 7.66(d, 1H, J=7.5Hz), 7.77(s, 1H), 7.93(d, 2H, J=7.5Hz), 10.24(brs, 1H), 12.12(brs, 1H), 12.56(brs, 1H)	ESI+ 508(100)

[0113]

[Table 27]

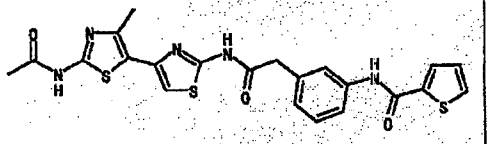
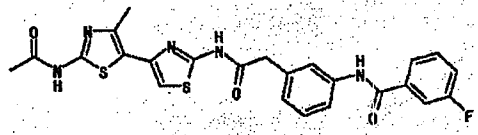
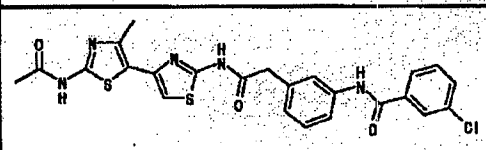
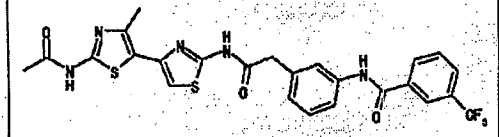
表 26

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
101	 C24H21N5O4S2	>90 結晶 >250	DMSO-d6, 300MH 2.12(s, 3H), 3.77(s, 2H), 4.56(d, 2H, J=5.5Hz), 5.21(t, 1H, J=5.5Hz), 7.06(d, 1H, J=7.7Hz), 7.30(t, 1H, J=7.7Hz), 7.35(s, 1H), 7.50-7.57(m, 3H), 7.66(d, 1H, J=7.5Hz), 7.77(s, 1H), 7.93(d, 2H, J=7.5Hz), 10.24(brs, 1H), 12.12(brs, 1H), 12.56(brs, 1H)	ESI+ 508(100)
102	 C29H32N6O3S2	>90 アモルファス	DMSO-d6-300 1.91(br, 2H), 2.12(s, 3H), 2.23(br, 6H), 2.35(br, 2H), 2.47(s, 3H), 4.19(s, 2H), 4.26(br, 2H), 7.05(d, 1H, J=7.7Hz), 7.27(s, 1H), 7.34(t, 1H, J=7.9Hz), 7.5-7.62(m, 3H), 7.71(d, 1H, J=7.9Hz), 7.75(s, 1H), 7.95(d, 2H, J=7Hz), 10.28(s, 2H), 12.05(s, 2H)	ESI+ 577(100)
103	 C25H24N4O3S2	>90 結晶 133 - 135.5	DMSO-d6-400 1.42(d, 3H, J=7Hz), 2.13(s, 3H), 2.45(s, 3H), 4.02(br, 1H), 5.62(br, 1H), 5.88(br, 1H), 7.18-7.35(m, 10H), 11.85(br, 1H), 12.34(br, 1H)	ESI+ 493(100)
104	 C22H19N5O4S2	>90 結晶 >220	DMSO-d6-300 2.13(s, 3H), 2.46(s, 3H), 3.78(s, 2H), 6.7(br, 1H), 7.02(d, 1H, J=7.76Hz), , 7.2(s, 1H), 7.25-7.33(m, 3H), 7.54(d, 1H, J=8.36Hz), , 7.73(s, 1H), 10.18(s, 1H), 12.06(s, 1H), 12.56(s, 1H)	ESI+ 482(100)

[0114]

[Table 28]

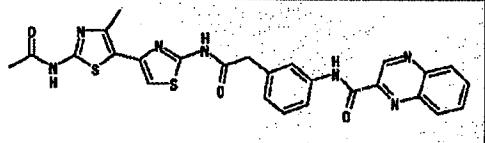
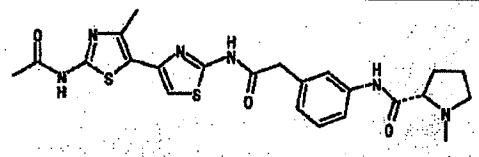
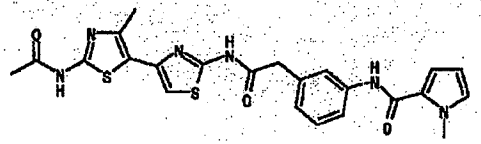
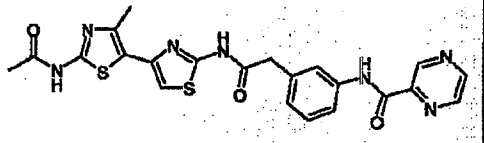
表 27

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
105	 C22H19N5O3S3	>90 結晶 >220	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.78(s, 2H), 7.02(d, 1H, J=7.76Hz), 7.2-7.39(m, 3H), 7.62-7.73(m, 2H), 7.81(br, 1H), 7.99(br, 1H), 10.18(s, 1H), 12.06(s, 1H), 12.56(s, 1H)	ESI+ 498(100)
106	 C24H20FN5O3S2	>90 結晶 175.4 - 177.1	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.78(s, 2H), 7.02(d, 1H, J=7.76Hz), 7.2(s, 1H), 7.3-7.45(m, 4H), 7.56-7.62(m, 1H), 7.67-7.71(m, 1H), 7.79-7.89(m, 1H), 10.29(s, 1H), 12.06(s, 1H), 12.56(s, 1H)	ESI+ 510(100)
107	 C24H20ClN5O3S2	>90 結晶 182 - 183.9	DMSO-d6-300 2.13(s, 3H), 2.46(s, 3H), 3.78(s, 2H), 7(d, 1H, J=7.68Hz), 7.2(s, 1H), 7.24(dd, 1H, J=7.68, 7.68Hz), 7.56-7.59(m, 1H), 7.77(s, 1H), 7.91(d, 1H, J=8.04Hz), , 8.01(s, 1H), 10.36(s, 1H), 12.06(s, 1H), 12.57(s, 1H)	ESI+ 526(100)
108	 C25H20F3N5O3S2	>90 結晶 171.7 - 173.4	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.78(s, 2H), 7.13(d, 1H, J=7.68Hz), 7.2(s, 1H), 7.24(dd, 1H, J=7.68, 7.68Hz), 7.66-7.79(m, 3H), 7.91(d, 1H, J=8.04Hz), 8.21-8.3(m, 2H), 10.46(s, 1H), 12.01(s, 1H), 12.57(s, 1H)	ESI+ 560(100)

[0115]

[Table 29]

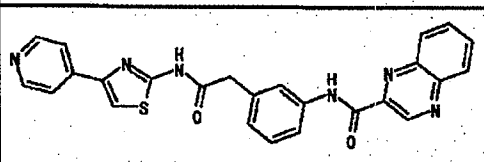
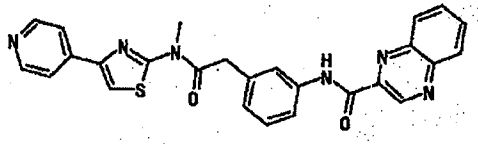
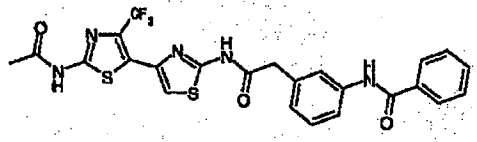
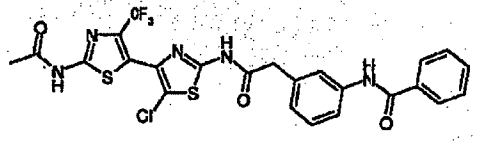
表 28

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
109	 C26H21N7O3S2	>90 結晶 >220	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.78(s, 2H), 7.16(d, 1H, J=7.68Hz), 7.21(s, 1H), 7.38(dd, 1H, J=7.68, 7.68Hz), 7.85(d, 1H, J=8.04Hz), 7.96(s, 1H), 8.01-8.04(m, 3H), 8.21-8.33(m, 3H), 9.55(s, 1H), 10.84(s, 1H), 12.06(s, 1H), 12.59(s, 1H)	ESI+ 544(100)
110	 C23H26N6O3S2	>90 結晶 >220	DMSO-d6-300 1.78(br, 3H), 2.13(br, 4H), 2.34(s, 4H), 2.46(s, 3H), 3.75(s, 2H), 7(d, 1H, J=7.68Hz), 7.2(s, 1H), 7.26(dd, 1H, J=7.68, 7.68Hz), 7.56(d, 1H, J=8.04Hz), 7.676(s, 1H), 9.67(s, 1H), 10.84(s, 1H), 12.06(s, 1H), 12.53(s, 1H)	ESI+ 499(100)
111	 C23H22N6O3S2	>90 結晶 >220	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.76(s, 2H), 3.87(s, 3H), 6.06(br, 1H), 6.95-7.14(m, 3H), 7.2(s, 1H), 7.26(dd, 1H, J=7.68, 7.68Hz), 7.56(d, 1H, J=8.04Hz), 7.67(s, 1H), 9.67(s, 1H), 12.06(s, 1H), 12.53(s, 1H)	ESI+ 495(100)
112	 C22H19N7O3S2	>90 結晶 >220	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.80(s, 2H), 3.87(s, 3H), 7.09(d, 1H, J=7.64Hz), 7.2(s, 1H), 7.34(dd, 1H, J=7.68, 7.68Hz), 7.56(d, 1H, J=8.04Hz), 7.93(s, 1H), 8.81(s, 1H), 8.92(s, 1H), 9.29(s, 1H), 10.71(s, 1H), 12.06(s, 1H), 12.56(s, 1H)	ESI+ 494(100)

[0116]

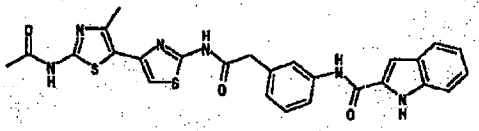
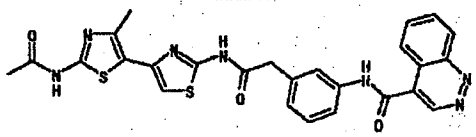
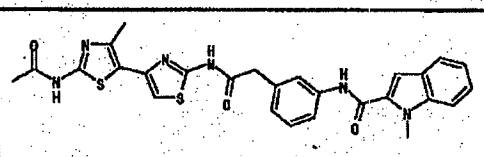
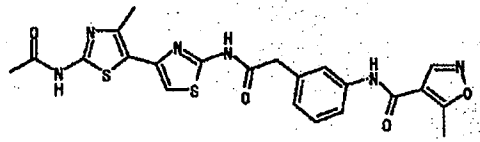
[Table 30]

表 29

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
113	 C25H18N6O2S	>90 結晶 253 – 255	DMSO-d6-300 3.86(s, 2H), 7.17(d, 1H, J=7.7Hz), 7.39(t, 1H, J=7.7Hz), 7.83–7.87(m, 3H), 7.97–8.05(m, 4H), 8.23(m, 1H), 8.31(m, 1H), 8.61–8.63(m, 2H), 9.55(s, 1H), 10.85(brs, 1H), 12.67(brs, 1H)	ESI+ 467(100)
114	 C26H20N6O2S	>90 結晶 250 – 252	DMSO-d6-300 3.86(s, 3H), 4.21(s, 2H), 7.11(d, 1H, J=7.7Hz), 7.40(t, 1H, J=7.7Hz), 7.85–7.90(m, 4H), 7.99–8.03(m, 3H), 8.22(m, 1H), 8.31(m, 1H), 8.60–8.62(m, 2H), 9.54(s, 1H), 10.84(brs, 1H)	ESI+ 481(100)
115	 C24H18F3N5O3S2	>90 結晶 160 – 163	DMSO-d6-300 2.19(s, 3H), 3.81(s, 2H), 7.1(d, 1H, J=7.7Hz), 7.33(t, 1H, J=7.9Hz), 7.45(s, 1H), 7.51–7.63(m, 3H), 7.7(d, 1H, J=7.7Hz), 7.8(s, 1H), 7.97(d, 2H, J=7.7Hz), 10.28(s, 1H), 12.63(s, 1H), 12.69(s, 1H)	ESI+ 546(100)
116	 C24H17ClF3N5O3S2	>80 結晶 >220	DMSO-d6-300 2.19(s, 3H), 3.81(s, 2H), 7.08(d, 1H, J=7.4Hz), 7.32(t, 1H, J=7.9Hz), 7.5–7.6(m, 3H), 7.69(d, 1H, J=7.9Hz), 7.78(s, 1H), 7.96(d, 2H, J=7.7Hz), 10.27(s, 1H), 12.78(s, 1H), 12.89(s, 1H)	ESI+ 580(100)

[0117]
[Table 31]

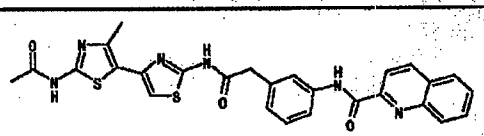
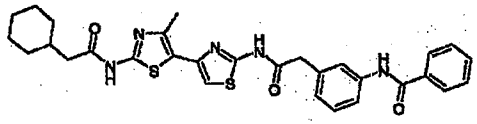
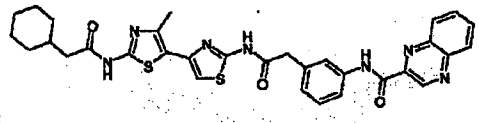
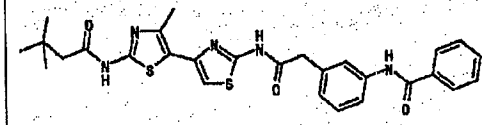
表 30

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
117	 C26H22N6O3S2	>90 結晶 201.8 - 204.4	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.80(s, 2H), 7.01-7.09(m, 2H), 7.19-7.2(m, 2H), 7.29-7.46(m, 3H), 7.62-7.75(m, 2H), 10.18(br, 1H), 11.66(br, 1H), 11.99(br, 1H), 12.51(br, 1H)	ESI+ 531(100)
118	 C26H21N7O3S2	>90 結晶 >250	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.80(s, 2H), 7.11-7.19(m, 2H), 7.32(dd, 1H, J=7.68, 7.68Hz), 7.67-7.69(m, 1H), 7.79(s, 1H), 7.95-8.06(m, 2H), 8.23-8.28(m, 1H), 8.59-8.61(m, 1H), 9.59(s, 1H), 10.91(s, 1H), 12.05(s, 1H), 12.58(s, 1H)	ESI+ 544(100)
119	 C27H24N6O3S2	>90 結晶 196.4 - 198.5	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.8(s, 2H), 4.02(s, 3H), 7.06-7.12(m, 2H), 7.2(s, 1H), 7.29-7.34(m, 3H), 7.52-7.54(m, 1H), 7.65-7.69(m, 2H), 7.81(s, 1H), 9.59(s, 1H), 10.31(s, 1H), 11.99(s, 1H), 12.58(s, 1H)	ESI+ 545(100)
120	 C22H20N6O4S2	>90 結晶 171.4 - 173.9	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.79(s, 2H), 7.10(d, 1H, J=7.56Hz), 7.2(s, 1H), 7.31(dd, 1H, J=7.88, 7.84Hz), 7.6(d, 1H, J=8.08Hz), 7.68(s, 1H), , 9.03(s, 1H), 10.01(s, 1H), 12.02(s, 1H), 12.51(s, 1H)	ESI+ 497(100)

[0118]

[Table 32]

表 31

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
121	 C27H22N6O3S2	>90 結晶 178.4 - 179.6	DMSO-d6-400 2.13(s, 3H), 2.46(s, 3H), 3.83(s, 2H), 7.10(d, 1H, J=7.56Hz), 7.2(s, 1H), 7.31(dd, 1H, J=7.88, 7.84Hz), 7.71-7.94(m, 4H), 8.09-8.12(m, 1H), 8.21-8.27(m, 2H), 8.61-8.64(m, 1H), 10.71(s, 1H), 11.98(s, 1H), 12.51(s, 1H)	ESI+ 543(100)
122	 C30H31N5O3S2	>90 アモルファス	DMSO-d6-300 0.90-1.29(m, 5H), 1.56-1.85(m, 6H), 2.30(d, 2H, J=7.0Hz), 2.47(s, 3H), 7.1(d, 1H, J=7.9Hz), 7.22(s, 1H), 7.33(t, 1H, J=7.9Hz), 7.51-7.63(m, 3H), 7.70(d, 1H, J=7.8Hz), 7.80(s, 1H), 7.97(d, 2H, J=7.9Hz), 10.28(br, 1H), 12.04(br, 1H), 12.58(br, 1H)	ESI+ 574(100)
123	 C32H31N7O3S2	>90 アモルファス	DMSO-d6-300 0.88-1.29(m, 5H), 1.56-1.85(m, 6H), 2.31(d, 2H, J=7Hz), 2.47(s, 3H), 3.85(s, 2H), 7.22(s, 1H), 7.40(t, 1H, J=7.85Hz), 7.87(d, 1H, J=8.1Hz), 7.97(s, 1H), 8.01-8.08(m, 2H), 8.22-8.37(m, 2H), 9.57(s, 1H), 10.86(s, 1H), 12.04(s, 1H), 12.61(s, 1H)	ESI+ 626(100)
124	 C28H29N5O3S2	>90 アモルファス	DMSO-d6-300 1.00(s, 9H), 2.28(s, 2H), 2.47(s, 3H), 3.80(s, 2H), 7.09(d, 1H, J=7.3Hz), 7.21(s, 1H), 7.31(t, 1H, J=7.7Hz), 7.49-7.60(m, 3H), 7.70(d, 1H, J=8.0Hz), 7.79(s, 1H), 7.95-7.97(m, 2H), 10.27(brs, 1H), 11.99(brs, 1H), 12.55(brs, 1H)	ESI+ 548(100)

[0119]

[Table 33]

表 32

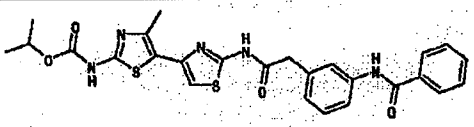
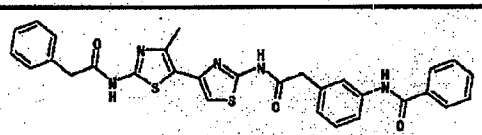
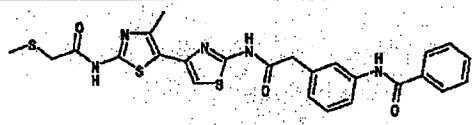
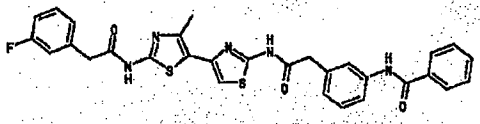
実施例番号	構造式 / 組成式	純度 (%) / 性状 / 融点 (℃)	1H NMR(δ)ppm	MS
125	 C26H25N5O4S2	>90 アモルファス	DMSO-d6-300 1.27(d, 6H, J=6.2Hz), 2.43(s, 3H), 3.80(s, 2H), 4.96(quint, 1H, J=6.2Hz), 7.09(d, 1H, J=7.3Hz), 7.18(s, 1H), 7.32(t, 1H, J=7.7Hz), 7.50-7.59(m, 3H), 7.70(d, 1H, J=8.0Hz), 7.79(s, 1H), 7.94-7.97(m, 2H), 10.26(brs, 1H), 11.55(brs, 1H), 12.55(brs, 1H)	ESI+ 536(100)
126	 C30H25N5O3S2	>90 アモルファス	DMSO-d6-300 2.47(s, 3H), 3.76(s, 2H), 3.79(s, 2H), 7.09(d, 1H, J=7.7Hz), 7.21(s, 1H), 7.28-7.34(m, 6H), 7.49-7.59(m, 3H), 7.68(d, 1H, J=8.0Hz), 7.78(s, 1H), 7.93-7.97(m, 2H), 10.26(brs, 1H), 12.33(brs, 1H), 12.56(brs, 1H)	ESI+ 568(100)
127	 C25H23N5O3S3	>90 アモルファス	DMSO-d6-300 2.15(s, 3H), 2.47(s, 3H), 3.37(s, 2H), 3.80(s, 2H), 7.09(d, 1H, J=7.7Hz), 7.23(s, 1H), 7.32(t, 1H, J=7.7Hz), 7.52-7.59(m, 3H), 7.69(d, 1H, J=8.0Hz), 7.79(s, 1H), 7.94-7.96(m, 2H), 10.26(brs, 1H), 12.19(brs, 1H), 12.57(brs, 1H)	ESI+ 538(100)
128	 C30H24FN5O3S2	>90 アモルファス	DMSO-d6-300 2.47(s, 3H), 3.79(s, 2H), 3.80(s, 2H), 7.07-7.19(m, 4H), 7.21(s, 1H), 7.28(t, 1H, J=7.7Hz), 7.37(m, 1H), 7.49-7.59(m, 3H), 7.68(d, 1H, J=8.0Hz), 7.78(s, 1H), 7.93-7.96(m, 2H), 10.25(brs, 1H), 12.34(brs, 1H), 12.56(brs, 1H)	ESI+ 586(100)

表 33

実施例番号	構造式／組成式	収度（%）／性状／融点（℃）	1H NMR(δ)ppm	MS
129	C29H29N5O3S2	>90 結晶 187.9 – 191.9	DMSO-d6-300 1.11–1.24(m, 2H), 1.45–1.79(m, 6H), 2.18–2.32(m, 1H), 2.42(d, 2H, J=7.7Hz), 2.47(s, 3H), 3.80(s, 2H), 7.10(d, 1H, J=7.4Hz), 7.22(s, 1H), 7.33(t, 1H, J=7.9Hz), 7.51–7.63(m, 3H), 7.70(d, 1H, J=7.9Hz), 7.81(s, 1H), 7.97(d, 2H, J=7.9Hz), 10.28(s, 1H), 12.04(s	ESI+ 560(100)
130	C29H27N5O3S2	>90 アモルファス	DMSO-d6-300 1.40–1.51(m, 1H), 1.97–2.08(m, 1H), 2.22–2.44(m, 4H), 2.47(s, 3H), 3.02–3.14(m, 1H), 5.67–5.73(m, 1H), 5.77–5.86(m, 1H), 7.10(d, 1H, J=7.9Hz), 7.22(s, 1H), 7.33(t, 1H, J=7.9Hz), 7.70(d, 1H, J=7.9Hz), 7.08(s, 1H), 7.97(d, 2H, J=7.9Hz), 10.28(s, 1H), 12.07(s	ESI+ 558(100)
131	C28H27N5O3S2	>90 アモルファス	DMSO-d6-300 1.50–1.93(m, 8H), 2.47(s, 3H), 2.83–2.95(m, 1H), 3.80(s, 2H), 7.10(d, 1H, J=7.9Hz), 7.21(s, 1H), 7.33(t, 1H, J=7.9Hz), 7.51–7.63(m, 3H), 7.70(d, 1H, J=7.9Hz), 7.80(s, 1H), 7.97(d, 2H, J=7.97Hz), 10.28(s, 1H), 12.05(s, 1H), 12.58(s, 1H)	ESI+ 546(100)
132	C29H22FN5O3S2	>90 結晶 140 dec.	DMSO-d6-300 2.53(s, 3H), 3.81(s, 2H), 7.28–7.48(m, 5H), 7.49–7.90(m, 7H), 7.95–7.99(m, 2H), 10.27(s, 1H), 12.51(s, 1H), 12.56(s, 1H)	ESI+ 572(100)

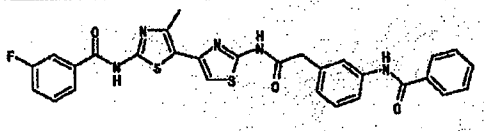
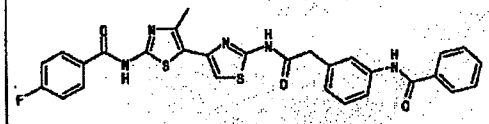
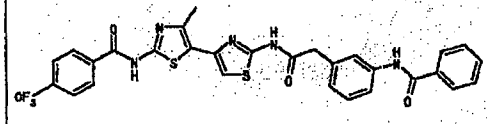
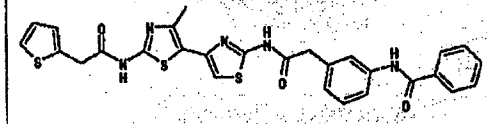
[0120]

[Table 34]

[0121]

[Table 35]

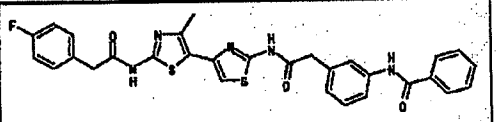
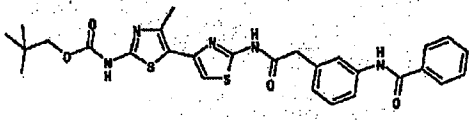
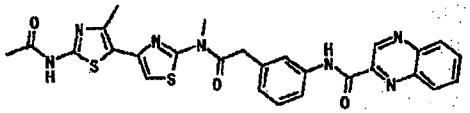
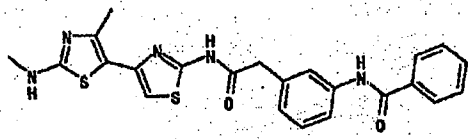
表 34

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
133	 C29H22FN5O3S2	>90 アモルファス	DMSO-d6-300 2.53(s, 3H), 3.81(s, 2H), 7.13(d, 1H, J=7.56Hz), 7.2(s, 1H), 7.34(dd, 1H, J=7.88, 7.84Hz), 7.49-7.61(m, 6H), 7.8(s, 1H), 7.94-7.97(m, 4H), 10.27(s, 1H), 12.51(s, 1H), 12.56(br, 1H)	ESI+ 572(100)
134	 C29H22FN5O3S2	>90 アモルファス	DMSO-d6-300 2.53(s, 3H), 3.81(s, 2H), 7.13(d, 1H, J=7.56Hz), 7.25(s, 1H), 7.32-7.4(m, 4H), 7.49-7.61(m, 4H), 7.80(s, 1H), 7.95-7.97(m, 2H), 8.14-8.22(m, 2H), 10.27(s, 1H), 12.54(br, 2H)	ESI+ 572(100)
135	 C30H22F3N5O3S2	>90 結晶 171.2 - 173.3	DMSO-d6-300 2.53(s, 3H), 3.81(s, 2H), 7.13(d, 1H, J=7.56Hz), 7.27(s, 1H), 7.34(dd, 1H, J=7.88, 7.84Hz), 7.49-7.61(m, 4H), 7.80(s, 1H), 7.95-7.97(m, 2H), 8.26-8.28(m, 2H), 10.27(s, 1H), 12.51(s, 1H), 12.9(br, 1H)	ESI+ 622(100)
136	 C28H23N5O3S3	>90 アモルファス	DMSO-d6-300 2.53(s, 3H), 3.79(s, 2H), 3.99(s, 2H), 6.92-7(m, 2H), 7.13(d, 1H, J=7.56Hz), 7.21(s, 1H), 7.34(dd, 1H, J=7.88, 7.84Hz), 7.36-7.39(m, 1H), 7.49-7.61(m, 4H), 7.80(s, 1H), 7.94-7.96(m, 2H), 10.26(s, 1H), 12.41(br, 1H), 12.56(br, 1H)	ESI+ 574(100)

[0122]

[Table 36]

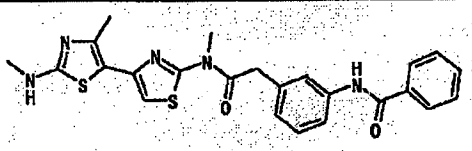
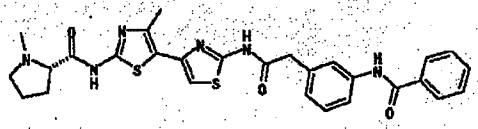
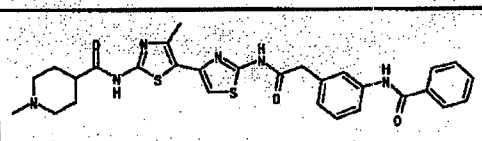
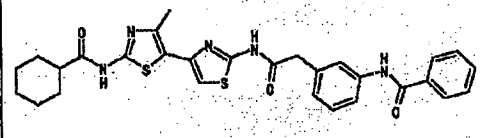
表 35

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
137	 C30H24FN5O3S2	>90 アモルファス	DMSO-d6-300 2.473(s, 3H), 3.75(s, 2H), 3.79(s, 2H), 7.05-7.21(m, 4H), 7.25-7.39(m, 3H), 7.49-7.61(m, 4H), 7.78(s, 1H), 7.94-7.96(m, 2H), 10.26(s, 1H), 12.32(s, 1H), 12.5(s, 1H)	ESI+ 586(100)
138	 C28H29N5O4S2	>90 結晶 158-160 dec.	DMSO-d6-400 0.94(s, 9H), 2.44(s, 3H), 3.79(s, 2H), 3.87(s, 2H), 7.08(d, 1H, J=7.7Hz), 718(s, 1H), 7.31(t, 1H, J=7.7Hz), 7.49-7.59(m, 3H), 7.70(d, 1H, J=7.9Hz), 7.79(s, 1H), 7.94-7.96(m, 2H), 10.24(brs, 1H), 11.65(brs, 1H), 12.53(brs, 1H)	ESI+ 564(100)
139	 C27H23N7O3S2	>90 結晶 159-161 dec.	DMSO-d6-400 2.14(s, 3H), 2.48(s, 3H), 3.80(s, 3H), 4.20(s, 2H), 7.11(d, 1H, J=7.7Hz), 7.26(s, 1H), 7.40(t, 1H, J=7.7Hz), 7.86(m, 1H), 7.89(s, 1H), 8.01-8.03(m, 2H), 8.23(m, 1H), 8.31(d, 1H, J=8.3Hz), 9.55(s, 1H), 10.82(brs, 1H), 12.03(brs, 1H)	ESI+ 558(100)
140	 C23H21N5O2S2	>90 アモルファス	DMSO-d6-400 2.37(s, 3H), 2.89(brs, 3H), 3.79(s, 2H), 7.06-7.10(m, 2H), 7.28(t, 1H, J=7.8Hz), 7.50-7.59(m, 3H), 7.66(d, 1H, J=8.5Hz), 7.79(s, 1H), 7.93-7.96(m, 2H), 10.24(brs, 1H), 12.49(brs, 1H)	ESI+ 464(100)

[0123]

[Table 37]

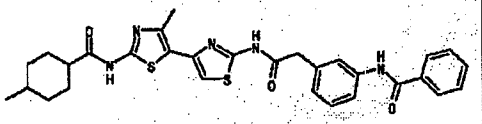
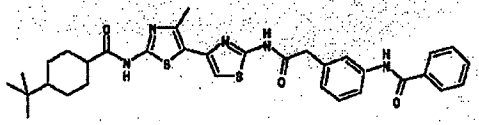
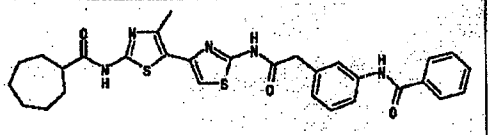
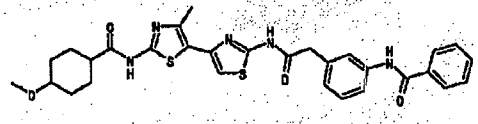
表 36

実施例番号	構造式 ／ 組成式	純度（%）／性状／融点（℃）	1H NMR(δ)ppm	MS
141	 C24H23N5O2S2	>90 アモルファス	DMSO-d6-400 2.40(s, 3H), 2.91(brs, 3H), 3.74(s, 3H), 4.15(s, 2H), 7.02(d, 1H, J=7.6Hz), 7.18(brs, 1H), 7.33(t, 1H, J=7.6Hz), 7.50-7.59(m, 3H), 7.69(d, 1H, J=8.0Hz), 7.74(s, 1H), 7.93-7.96(m, 2H), 10.25(brs, 1H)	ESI+ 478(100)
142	 C28H28N6O3S2	>90 アモルファス	DMSO-d6-400 1.8(br, 3H), 2.12(br, 1H), 2.33(br, 4H), 2.47(s, 3H), 3.09(br, 2H), 3.8(s, 2H), 7.09(d, 1H, J=7.68Hz), 7.23(s, 1H), 7.31(dd, 1H, J=7.88, 7.84Hz), 7.5-7.59(m, 3H), 7.68(d, 1H, J=7.92Hz), 7.79(s, 1H), 7.95(d, 2H, J=7.08Hz), 10.24(s, 1H), 11.5(s, 1H), 12.55(	ESI+ 561(100)
143	 C29H30N6O3S2	>90 アモルファス	DMSO-d6-400 1.64-1.93(m, 6H), 2.19(s, 3H), 2.43(br, 1H), 2.47(s, 3H), 2.82(br, 2H), 3.8(s, 2H), 7.09(d, 1H, J=7.68Hz), 7.23(s, 1H), 7.31(dd, 1H, J=7.88, 7.84Hz), 7.5-7.59(m, 3H), 7.68(d, 1H, J=7.92Hz), 7.79(s, 1H), 7.95(d, 2H, J=7.08Hz), 10.24(s, 1H), 12.02(s, 1H), 1	ESI+ 575(100)
144	 C29H29N5O3S2	>90 アモルファス	DMSO-d6-400 1.11(br, 5H), 1.39-1.42(m, 2H), 1.66-1.82(m, 4H), 2.46(s, 3H), 3.8(s, 2H), 7.09(d, 1H, J=7.68Hz), 7.19(s, 1H), 7.31(dd, 1H, J=7.88, 7.84Hz), 7.5-7.59(m, 3H), 7.68(d, 1H, J=7.92Hz), 7.79(s, 1H), 7.95(d, 2H, J=7.08Hz), 10.24(s, 1H), 11.93(s, 1H), 12.54(s, 1	ESI+ 560(100)

[0124]

[Table 38]

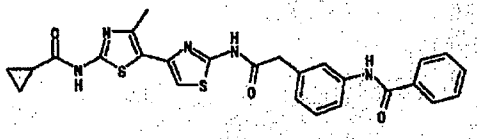
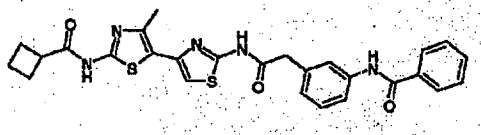
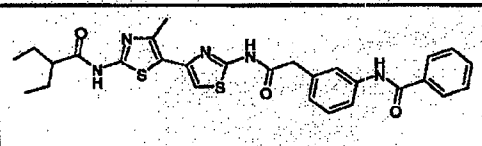
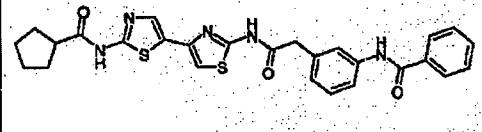
表 37

実施例番号	構造式 ／組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
145	 C30H31N5O3S2	>90 結晶 150.5 - 153.2	DMSO-d6-400 0.89(d, 3Hx1/2, J=6.52Hz), 0.92(d, 3Hx1/2, J=6.96Hz), 1.4-1.59(m, 5H), 1.78-1.84(m, 3H), 2.46(s, 3H), 3.6(s, 2H), 7.09(d, 1H, J=7.68Hz), 7.19(s, 1H), 7.31(dd, 1H, J=7.88, 7.84Hz), 7.5-7.59(m, 3H), 7.68(d, 1H, J=7.92Hz), 7.79(s, 1H), 7.95(d, 2H, J=7.08Hz),	ESI+ 574(100)
146	 C33H37N5O3S2	>90 結晶 151.9 - 154.8	DMSO-d6-300 0.8-1.12(m, 12H), 1.35-1.59(m, 5H), 1.78-1.93(m, 3H), 2.08(br, 1H), 2.46(s, 3H), 3.8(s, 2H), 7.09(d, 1H, J=7.68Hz), 7.19(s, 1H), 7.31(dd, 1H, J=7.88, 7.84Hz), 7.5-7.59(m, 3H), 7.68(d, 1H, J=7.92Hz), 7.79(s, 1H), 7.95(d, 2H, J=7.08Hz), 10.26(s, 1H), 11.93(	ESI+ 616(100)
147	 C30H31N5O3S2	>90 結晶 158.5 - 160.5	DMSO-d6-400 1.48-1.67(m, 10H), 1.84(br, 2H), 2.64-2.67(m, 1H), 2.46(s, 3H), 3.8(s, 2H), 7.09(d, 1H, J=7.68Hz), 7.19(s, 1H), 7.31(dd, 1H, J=7.88, 7.84Hz), 7.5-7.59(m, 3H), 7.68(d, 1H, J=7.92Hz), 7.79(s, 1H), 7.95(d, 2H, J=7.08Hz), 10.24(s, 1H), 11.92(s, 1H), 12.53(s,	ESI+ 574(100)
148	 C30H31N5O4S2	>90 アモルファス	DMSO-d6-400 1.21-1.67(m, 6H), 1.87(br, 2H), 2.05(br, 1H), 2.46(s, 3H), 3.21(s, 3Hx1/2), 3.24(s, 3Hx1/2), 3.8(s, 2H), 7.09(d, 1H, J=7.68Hz), 7.19(s, 1H), 7.31(dd, 1H, J=7.88, 7.84Hz), 7.5-7.59(m, 3H), 7.68(d, 1H, J=7.92Hz), 7.79(s, 1H), 7.95(d, 2H, J=7.08Hz), 10.24(s,	ESI+ 590(100)

[0125]

[Table 39]

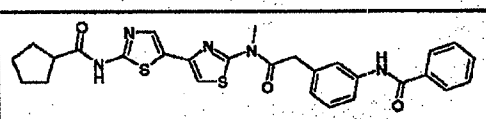
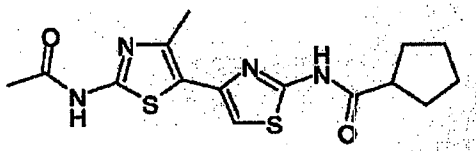
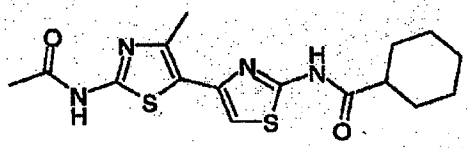
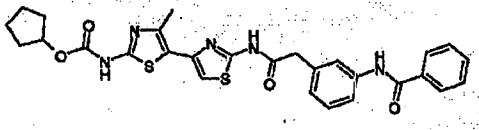
表 38

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
149	 C26H23N5O3S2	>90 結晶 >220	DMSO-d6-300 0.87-0.95(m, 4H), 1.87-1.98(m, 1H), 2.47(s, 3H), 3.08(s, 2H), 7.10(d, 1H, J=7.7Hz), 7.21(s, 1H), 7.32(t, 1H, J=7.9Hz), 7.51-7.63(m, 3H), 7.70(d, 1H, J=8.0Hz), 7.80(s, 1H), 7.97(d, 2H, J=7.9Hz), 10.28(s, 1H), 12.36(s, 1H), 12.58(s, 1H)	ESI+ 518(100)
150	 C27H25N5O3S2	>90 アモルファス	DMSO-d6-300 1.75-2.29(m, 7H), 2.46(s, 3H), 3.81(s, 3H), 7.10(d, 1H, J=7.7Hz), 7.22(s, 1H), 7.33(t, 1H, J=7.7Hz), 7.50-7.63(m, 3H), 7.07(d, 1H, J=7.9Hz), 7.80(s, 1H), 7.97(d, 2H, J=7.9Hz), 10.28(s, 1H), 11.94(s, 1H), 12.59(s, 1H)	ESI+ 532(100)
151	 C28H29N5O3S2	>90 アモルファス	DMSO-d6-300 0.82(t, 6H, J=7.5Hz), 1.43-1.63(m, 4H), 2.36-2.46(m, 1H), 2.48(s, 3H), 3.81(s, 2H), 7.10(d, 1H, J=7.9Hz), 7.22(s, 1H), 7.33(t, 1H, J=7.9Hz), 7.51-7.62(m, 3H), 7.71(d, 1H, J=7.9Hz), 7.81(s, 1H), 7.97(d, 2H, J=7.9Hz), 10.28(s, 1H), 12.10(s, 1H), 12.58(s, 1H	ESI+ 548(100)
152	 C27H25N5O3S2	>90 結晶 >220	DMSO-d6-300 1.49-1.98(m, 8H), 2.87-3.02(m, 1H), 3.80(s, 2H), 7.10(d, 1H, J=7.9Hz), 7.33(t, 1H, J=7.9Hz), 7.44(s, 1H), 7.52-7.63(m, 3H), 7.70(d, 1H, J=8.0Hz), 7.80(s, 1H), 7.84(s, 1H), 7.97(d, 2H, J=7.8Hz), 10.28(s, 1H), 12.14(s, 1H), 12.63(s, 1H)	ESI+ 532(100)

[0126]

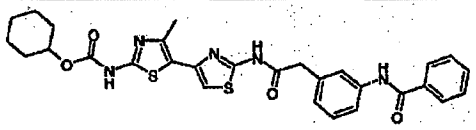
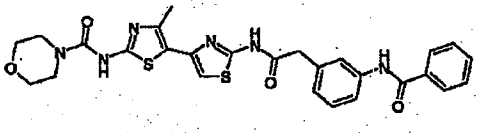
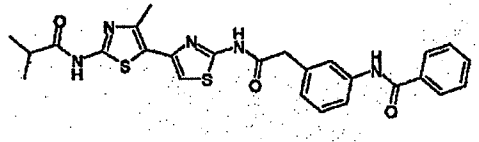
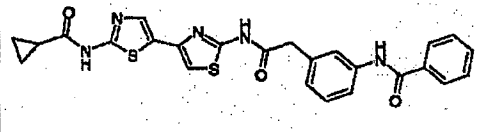
[Table 40]

表 39

実施例番号	構造式 / 組成式	純度 (%) / 性状 / 融点 (℃)	1H NMR(δ)ppm	MS
153	 C28H27N5O3S2	>90 結晶 188-192 dec.	DMSO-d6-300 1.48-1.96(m, 8H), 2.88-2.99(m, 1H), 3.79(s, 3H), 4.16(s, 2H), 7.05(d, 1H, J=7.3Hz), 7.35(t, 1H, J=7.7Hz), 7.47(s, 1H), 7.51-7.62(m, 3H), 7.72(d, 1H, J=7.3Hz), 7.74(br, 1H), 7.86(br, 1H), 7.97(d, 2H, J=7.3Hz), 10.28(s, 1H), 12.15(s, 1H)	ESI+ 546(100)
154	 C15H18N4O2S2	>90 結晶 212-215 dec.	DMSO-d6-400 1.49-1.93(m, 8H), 2.13(s, 3H), 2.46(s, 3H), 2.9-2.98(m, 1H), 7.18(s, 1H), 12.03(s, 1H), 12.21(s, 1H)	ESI+ 351(100)
155	 C16H20N4O2S2	>90 アモルファス	DMSO-d6-400 1.17-1.46(m, 5H), 1.62-1.86(m, 5H), 2.13(s, 3H), 2.46(s, 3H), 2.46-2.57(m, 1H), 7.17(s, 1H), 12.03(s, 1H), 12.15(s, 1H)	ESI+ 365(100)
156	 C28H27N5O4S2	>90 アモルファス	DMSO-d6-400 1.51-1.95(m, 8H), 2.42(s, 3H), 3.80(s, 2H), 5.15(br, 1H), 7.09(d, 1H, J=7.9Hz), 7.18(s, 1H), 7.32(t, 1H, J=7.9Hz), 7.50-7.62(m, 3H), 7.69(d, 1H, J=8.4Hz), 7.78(s, 1H), 7.96(d, 2H, J=8.3Hz), 10.25(s, 1H), 11.51(s, 1H), 12.53(s, 1H)	ESI+ 562(100)

[0127]
[Table 41]

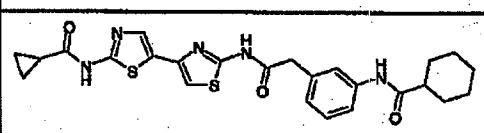
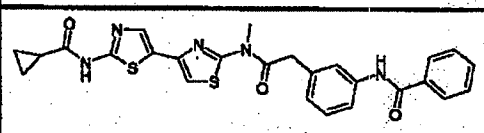
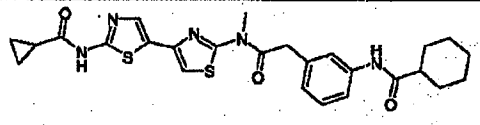
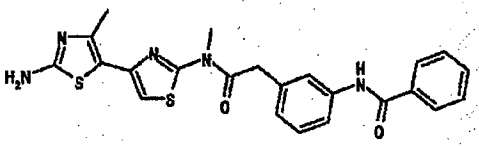
表 40

実施例番号	構造式 / 組成式	純度 (%) / 性状 / 融点 (°C)	1H NMR(δ)ppm	MS
157	 C29H29N5O4S2	>90 アモルファス	DMSO-d6-300 1.18-1.56(m, 6H), 1.66-1.77(m, 2H), 1.83-1.94(m, 2H), 2.43(s, 3H), 3.80(s, 2H), 4.70(br, 1H), 7.10(d, 1H, J=7.7Hz), 7.19(s, 1H), 7.33(t, 1H, J=7.7Hz), 7.51-7.60(m, 3H), 7.70(d, 1H, J=8.5Hz), 7.80(s, 1H), 7.97(d, 2H, J=8.5Hz), 10.28(s, 1H), 11.59(s, 1H), 1	ESI+ 576(100)
158	 C27H26N6O4S2	>90 アモルファス	DMSO-d6-300 2.43(s, 3H), 3.45-3.64(m, 8H), 3.80(s, 2H), 7.10(d, 1H, J=7.7Hz), 7.14(s, 1H), 7.33(t, 1H, J=8.1Hz), 7.51-7.62(m, 3H), 7.70(d, 1H, J=8.5Hz), 7.80(s, 1H), 7.97(d, 2H, J=8.5Hz), 10.28(s, 1H), 10.90(s, 1H), 12.56(s, 1H)	ESI+ 563(10)
159	 C26H25N5O3S2	>90 アモルファス	DMSO-d6-400 1.12(d, 6H, J=6.6Hz), 2.47(s, 3H), 2.67-2.76(m, 1H), 3.80(s, 2H), 7.09(d, 1H, J=7.6Hz), 7.20(s, 1H), 7.32(t, 1H, J=7.85Hz), 7.51-7.61(m, 3H), 7.69(d, 1H, J=7.6Hz), 7.79(s, 1H), 7.95(d, 3H, J=7.9Hz), 10.25(s, 1H), 11.99(s, 1H), 12.55(s, 1H)	ESI+ 520(100)
160	 C25H21N5O3S2	>90 結晶 >220	DMSO-d6-400 0.87-0.96(m, 4H), 1.94-2.00(m, 1H), 3.79(s, 2H), 7.09(d, 1H, J=7.6Hz), 7.31(t, 1H, J=7.9Hz), 7.41(s, 1H), 7.50-7.61(m, 3H), 7.69(d, 1H, J=8.1Hz), 7.78(s, 1H), 7.82(s, 1H), 7.96(d, 2H, J=7.6Hz), 10.24(s, 1H), 12.39(s, 1H), 12.58(s, 1H)	ESI+ 504(100)

[0128]

[Table 42]

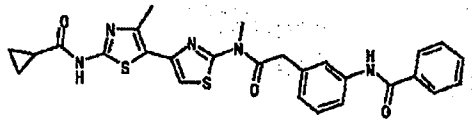
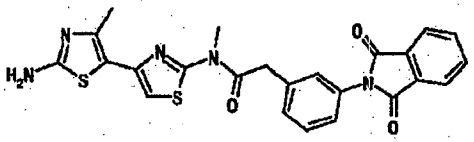
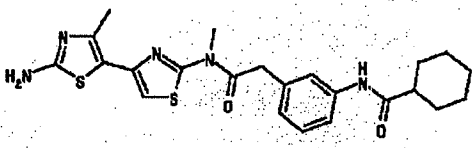
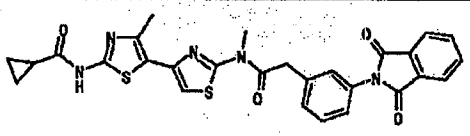
表 41

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
161	 C25H27N5O3S2	>90 結晶 >220	DMSO-d6-400 0.88-0.98(m, 4H), 1.14-1.47(m, 5H), 1.62-1.83(m, 5H), 1.94-2.01(m, 1H), 2.28-2.36(m, 1H), 3.74(s, 2H), 6.99(d, 1H, J=7.7Hz), 7.23(t, 1H, J=7.7Hz), 7.41(s, 1H), 7.50(d, 1H, J=7.7Hz), 7.61(s, 1H), 7.82(s, 1H), 9.78(s, 1H), 12.40(s, 1H), 12.56(s, 1H)	ESI+ 510(100)
162	 C26H23N5O3S2	>90 結晶 >220	DMSO-d6-300 0.86-0.99(m, 4H), 1.93-2.01(m, 1H), 3.79(s, 3H), 4.16(s, 2H), 7.05(d, 1H, J=7.6Hz), 7.35(t, 1H, J=7.6Hz), 7.47(s, 1H), 7.49-7.63(m, 3H), 7.72(d, 1H, J=7.6Hz), 7.74(s, 1H), 7.88(s, 1H), 7.97(d, 2H, J=7.8Hz), 10.29(s, 1H), 12.45(s, 1H)	ESI+ 518(100)
163	 C26H29N5O3S2	>90 結晶 >220	DMSO-d6-300 0.83(m, 4H), 1.14-1.48(m, 5H), 1.59-1.99(m, 6H), 2.26-2.38(m, 1H), 3.75(s, 3H), 4.10(s, 2H), 6.95(d, 1H, J=7.8Hz), 7.26(t, 1H, J=7.8Hz), 7.44(s, 1H), 7.53(d, 1H, J=7.8Hz), 7.55(s, 1H), 7.85(s, 1H), 9.81(s, 1H), 12.45(s, 1H)	ESI+ 524(100)
164	 C23H21N5O2S2	>90 結晶 219-221 dec.	DMSO-d6-400 2.32(s, 3H), 3.74(s, 3H), 4.13(s, 2H), 6.93(brs, 2H), 6.95(s, 1H), 7.02(d, 1H, J=7.7Hz), 7.35(t, 1H, J=7.7Hz), 7.50-7.59(m, 3H), 7.71(m, 1H), 7.73(s, 1H), 7.93-7.96(m, 2H), 10.22(brs, 1H)	ESI+ 464(100)

[0129]

[Table 43]

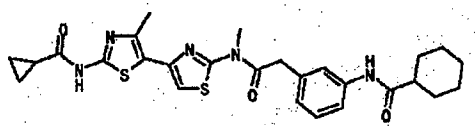
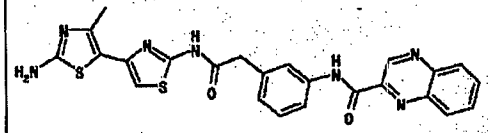
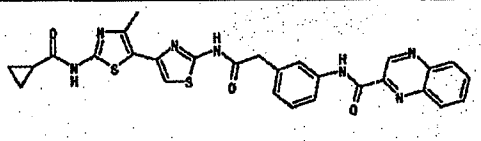
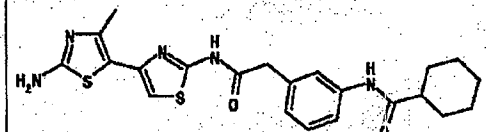
表 42

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
165	 C27H25N5O3S2	>90 結晶 241-243 dec.	DMSO-d6-300 0.87-0.91(m, 4H), 1.91(m, 1H), 2.46(s, 3H), 3.75(s, 3H), 4.14(s, 2H), 7.02(d, 1H, J=7.4Hz), 7.23(s, 1H), 7.32(t, 1H, J=7.4Hz), 7.48-7.57(m, 3H), 7.68(m, 1H), 7.71(s, 1H), 7.92-7.95(m, 2H), 10.25(brs, 1H), 12.33(brs, 1H)	ESI+ 532(100)
166	 C24H19N5O3S2	>90 結晶 188-190 dec.	DMSO-d6-300 2.30(s, 3H), 3.75(s, 3H), 4.20(s, 2H), 6.93(s, 1H), 6.94(brs, 2H), 7.33-7.50(m, 3H), 7.48(m, 1H), 7.87-7.97(m, 4H)	ESI+ 490(100)
167	 C23H27N5O2S2	>90 結晶 168-170 dec.	DMSO-d6-400 1.14-1.41(m, 5H), 1.65(m, 1H), 1.72-1.80(m, 4H), 2.31(s, 3H), 2.31(m, 1H), 3.71(s, 3H), 4.07(s, 2H), 6.92(brs, 2H), 6.95(m, 1H), 7.50(t, 1H, J=7.7Hz), 7.51(m, 1H), 7.53(s, 1H), 9.77(brs, 1H)	ESI+ 470(100)
168	 C28H23N5O4S2	>90 結晶 225 - 227	DMSO-d6-300 0.87-0.91(m, 4H), 1.91(m, 1H), 2.47(s, 3H), 3.78(s, 3H), 4.23(s, 2H), 7.24(s, 1H), 7.35-7.37(m, 3H), 7.50(m, 1H), 7.88-7.98(m, 4H), 12.33(brs, 1H)	ESI+ 558(100)

[0130]

[Table 44]

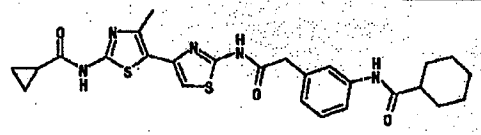
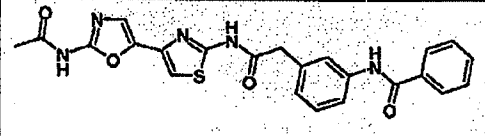
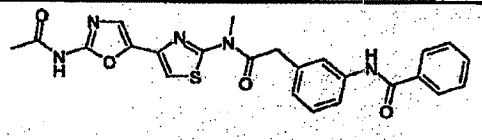
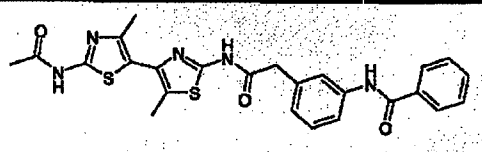
表 43

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
169	 C27H31N5O3S2	>90 アモルファス	DMSO-d6-300 0.87-0.91(m, 4H), 1.14-1.41(m, 5H), 1.64(m, 1H), 1.72-1.79(m, 4H), 1.91(m, 1H), 2.31(m, 1H), 2.47(s, 3H), 3.73(s, 3H), 4.08(s, 2H), 6.92(d, 1H, J=7.4Hz), 7.20-7.26(m, 2H), 7.50(m, 1H), 7.52(s, 1H), 9.78(brs, 1H), 12.32(brs, 1H)	ESI+ 538(100)
170	 C24H19N7O2S2	>90 結晶 174.8 - 176.1	DMSO-d6-300 2.3(s, 3H), 3.8(s, 2H), 6.93(s, 1H), 6.95(s, 2H), 7.16(d, 1H, J=7.68Hz), 7.38(dd, 1H, J=7.88, 7.84Hz), 7.68(d, 1H, J=7.92Hz), 7.95(s, 1H), 8.01-8.04(m, 2H), 8.21-8.33(m, 3H), 9.55(s, 1H), 10.84(s, 1H), 12.47(s, 1H)	ESI+ 502(100)
171	 C28H23N7O3S2	>90 結晶 196.3 - 199	DMSO-d6-400 0.89-0.9(m, 4H), 1.93(br, 1H), 2.49(s, 3H), 3.84(s, 2H), 7.16(d, 1H, J=7.64Hz), 7.2(s, 1H), 7.38(dd, 1H, J=7.88, 7.84Hz), 7.85(d, 1H, J=8.16Hz), 7.95(s, 1H), 8.01-8.03(m, 2H), 8.22-8.24(m, 2H), 8.29-8.32(m, 2H), 9.55(s, 1H), 10.82(s, 1H), 12.31(s, 1H), 12	ESI+ 570(100)
172	 C22H25N5O2S2	>90 結晶 >220	DMSO-d6-400 1.16-1.42(m, 5H), 1.66-1.79(m, 5H), 2.29(s, 3H), 2.31(br, 1H), 3.72(s, 1H), 6.91(s, 2H), 6.93(s, 1H), 6.98(d, 1H, J=7.56Hz), 7.22(dd, 1H, J=7.92, 7.8Hz), 7.48(d, 1H, J=8.36Hz), 7.6(s, 1H), 9.77(s, 1H), 12.99(s, 1H)	ESI+ 456(100)

[0131]

[Table 45]

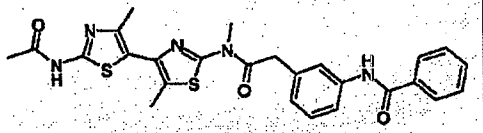
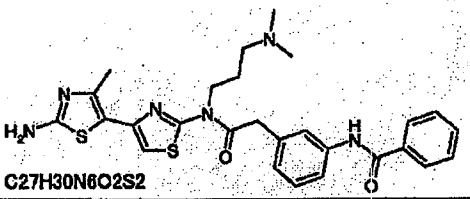
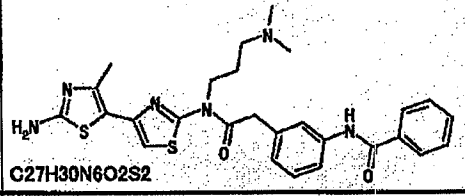
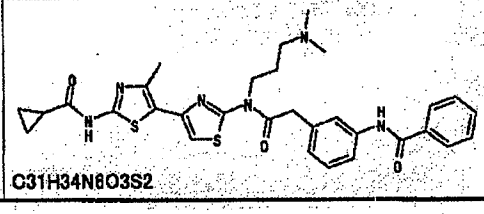
表 44

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
173	 C26H29N5O3S2	>90 結晶 >220	DMSO-d6-400 0.89-0.9(m, 4H), 1.16-1.42(m, 5H), 1.66-1.79(m, 5H), 1.93(br, 1H), 2.29(s, 3H), 2.32(br, 1H), 3.73(s, 1H), 6.98(d, 1H, J=7.56Hz), 7.19(s, 1H,)7.22(dd, 1H, J=7.92, 7.8Hz), 7.48(d, 1H, J=8.36Hz), 7.6(s, 1H), 9.77(s, 1H), 12.31(s, 1H), 12.5(s, 1H)	ESI+ 524(100)
174	 C23H19N5O4S	>90 アモルファス	DMSO-d6-300 2.12(s, 3H), 3.79(s, 2H), 7.1(d, 1H, J=7.7Hz), 7.25(s, 1H), 7.27(s, 1H), 7.33(t, 1H, J=7.9Hz), 7.51-7.63(m, 3H), 7.70(d, 1H, J=7.9Hz), 7.80(s, 1H), 7.97(d, 2H, J=6.6Hz), 10.28(s, 1H), 11.30(s, 1H), 12.72(s, 1H), 7.25(s, 1H), 7.27(s, 1H)	ESI+ 462(100)
175	 C24H21N5O4S	>90 アモルファス	DMSO-d6-300 2.11(s, 3H), 3.78(s, 3H), 4.16(s, 2H), 7.04(d, 1H, J=8.1Hz), 7.31-7.36(m, 3H), 7.49-7.63(m, 3H), 7.71(d, 1H, J=7.9Hz), 7.74(s, 1H), 7.96(d, 2H, J=6.6Hz), 10.27(s, 1H), 11.27(s, 1H)	ESI+ 476(100)
176	 C25H23N5O3S2	>90 アモルファス	DMSO-d6-300 2.14(s, 3H), 2.23(s, 3H), 2.29(s, 3H), 3.76(s, 2H), 7.09(d, 1H, J=7.9Hz), 7.32(t, 1H, J=7.9Hz), 7.51-7.62(m, 3H), 7.70(d, 1H, J=7.9Hz), 7.79(s, 1H), 7.97(d, 2H, J=6.9Hz), 10.28(s, 1H), 12.10(s, 1H), 12.39(s, 1H)	ESI+ 506(100)

[0132]

[Table 46]

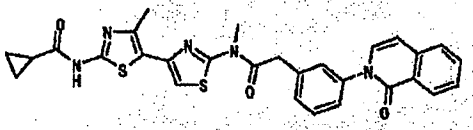
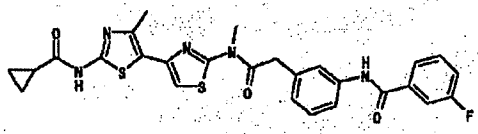
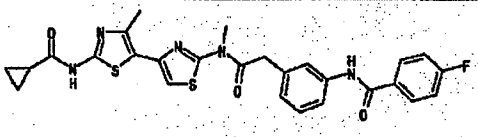
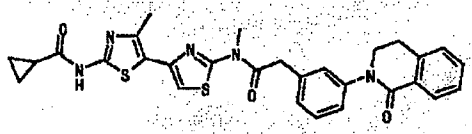
表 45

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
177	 C26H25N5O3S2	>90 結晶 >220	DMSO-d6-300 2.14(s, 3H), 2.25(s, 3H), 2.31(s, 3H), 3.69(s, 3H), 4.13(s, 2H), 7.04(d, 1H, J=7.7Hz), 7.34(t, 1H, J=7.7Hz), 7.51-7.63(m, 3H), 7.72(d, 1H, J=7.7Hz), 7.73(s, 1H), 7.97(d, 2H, J=9.5Hz), 10.28(s, 1H), 12.09(s, 1H)	ESI+ 520(100)
178	 C27H30N6O2S2	>90 結晶	DMSO-d6-400 1.85-1.87(m, 2H), 2.17(s, 6H), 2.30-2.32(m, 2H), 2.31(s, 3H), 4.11(s, 2H), 4.20-4.22(m, 2H), 6.93(brs, 2H), 6.95(s, 1H), 7.03(d, 1H, J=7.5Hz), 7.33(t, 1H, J=7.5Hz), 7.50-7.58(m, 3H), 7.70(m, 1H), 7.73(s, 1H), 7.94-7.95(m, 2H), 10.25(brs, 1H)	ESI+ 535(100)
179	 C27H30N6O2S2	>90 結晶 180 - 182	DMSO-d6-400 1.85-1.87(m, 2H), 2.17(s, 6H), 2.30-2.32(m, 2H), 2.31(s, 3H), 4.11(s, 2H), 4.20-4.22(m, 2H), 6.93(brs, 2H), 6.95(s, 1H), 7.03(d, 1H, J=7.5Hz), 7.33(t, 1H, J=7.5Hz), 7.50-7.58(m, 3H), 7.70(m, 1H), 7.73(s, 1H), 7.94-7.95(m, 2H), 10.25(brs, 1H)	ESI+ 535(100)
180	 C31H34N6O3S2	>90 結晶 167 - 171	DMSO-d6-300 0.87-0.91(m, 4H), 1.88-1.91(m, 3H), 2.15(s, 6H), 2.25-2.31(m, 2H), 2.47(s, 3H), 4.19(s, 2H), 4.21-4.24(m, 2H), 7.03(d, 1H, J=7.5Hz), 7.23(s, 1H), 7.32(t, 1H, J=7.5Hz), 7.49-7.58(m, 3H), 7.69(m, 1H), 7.72(s, 1H), 7.91-7.95(m, 2H), 10.25(brs, 1H), 12.31(brs	ESI+ 603(100)

[0133]

[Table 47]

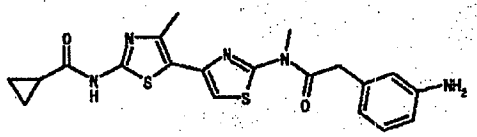
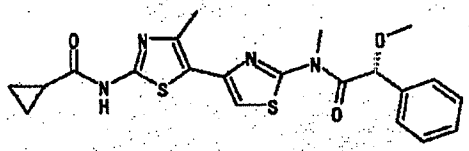
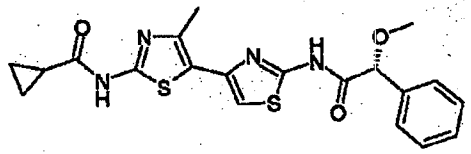
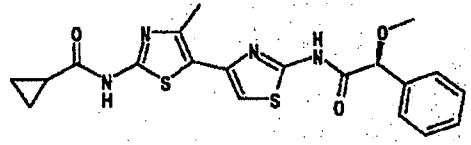
表 46

実施例番号	構造式 / 組成式	純度(%) / 性状 / 融点(℃)	1H NMR(δ)ppm	MS
181	 C29H25N5O3S2	>90 結晶 >250	DMSO-d6-300 0.88-0.92(m, 4H), 1.92(m, 1H), 2.48(s, 3H), 3.80(s, 3H), 4.24(s, 2H), 6.73(d, 1H, J=7.7Hz), 7.25(s, 1H), 7.38-7.56(m, 6H), 7.74(s, 1H), 7.77(m, 1H), 8.26(d, 1H, J=8.0Hz), 12.34(brs, 1H)	ESI+ 556(100)
182	 C27H24FN5O3S2	>90 結晶 >220	DMSO-d6-300 0.89-0.9(m, 4H), 1.93(br, 1H), 2.48(s, 3H), 3.77(s, 3H), 4.16(s, 2H), 7(d, 1H, J=7.68Hz), 7.25(s, 1H), 7.35(dd, 1H, J=7.88, 7.84Hz), 7.38-7.42(m, 1H), 7.56-7.65(m, 1H), 7.78-7.83(m, 4H), 10.33(s, 1H), 12.35(m, 1H)	ESI+ 550(100)
183	 C27H24FN5O3S2	>90 結晶 190.5 - 192.4	DMSO-d6-300 0.89-0.9(m, 4H), 1.93(br, 1H), 2.48(s, 3H), 3.77(s, 3H), 4.15(s, 2H), 7.(d, 1H, J=7.68Hz), 7.25(s, 1H), 7.33-7.39(m, 3H), 7.68-7.7(m, 2H), 8.01-8.06(m, 2H), 10.28(s, 1H), 12.34(s, 1H)	ESI+ 550(100)
184	 C29H27N5O3S2	>90 結晶 249-251 dec.	DMSO-d6-300 0.88-0.91(m, 4H), 1.92(m, 1H), 2.46(s, 3H), 3.12(t, 2H, J=6.6Hz), 3.77(s, 3H), 3.95(t, 2H, J=6.6Hz), 4.17(s, 2H), 7.17(d, 1H, J=7.3Hz), 7.23(s, 1H), 7.34-7.40(m, 5H), 7.50(m, 1H), 7.93(d, 1H, J=8.0Hz), 12.33(brs, 1H)	ESI+ 558(100)

[0134]

[Table 48]

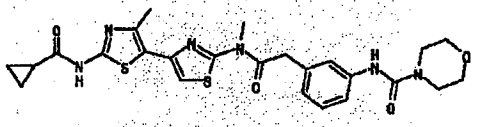
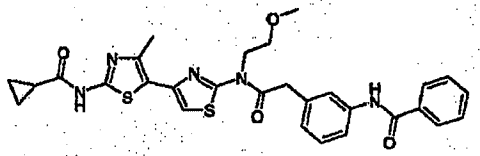
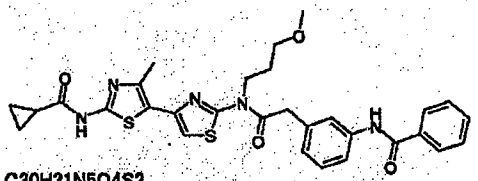
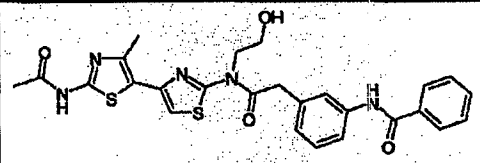
表 47

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
185	 C20H21N5O2S2	>90 結晶 >220	DMSO-d6-300 0.89-0.9(m, 4H), 1.93(br, 1H), 2.47(s, 3H), 3.69(s, 3H), 3.94(s, 2H), 5.06(s, 2H), 6.42-6.49(m, 3H), 6.92-7.02(m, 1H), 7.24(s, 1H), 12.34(s, 1H)	ESI+ 428(100)
186	 C21H22N4O3S2	>90 結晶 201.4 dec.	DMSO-d6-400 0.89-0.9(m, 4H), 1.93(br, 1H), 2.46(s, 3H), 3.36(s, 3H), 3.61(s, 3H), 5.66(s, 1H), 7.22(s, 1H), 7.46-7.61(m, 5H), 12.31(s, 1H)	ESI+ 443(100)
187	 C20H20N4O3S2	>90 結晶 212 dec.	DMSO-d6-400 0.89-0.9(m, 4H), 1.93(br, 1H), 2.46(s, 3H), 3.34(s, 3H), 5.05(s, 1H), 7.22(s, 1H), 7.34-7.52(m, 5H), 12.33(s, 1H), 12.54(s, 1H)	ESI+ 429(100)
188	 C20H20N4O3S2	>90 結晶 215.9 dec.	DMSO-d6-300 0.89-0.9(m, 4H), 1.93(br, 1H), 2.46(s, 3H), 3.34(s, 3H), 5.05(s, 1H), 7.22(s, 1H), 7.34-7.52(m, 5H), 12.33(s, 1H), 12.54(s, 1H)	ESI+ 429(100)

[0135]

[Table 49]

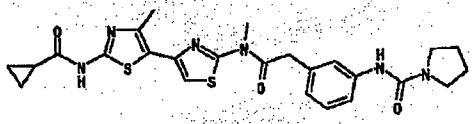
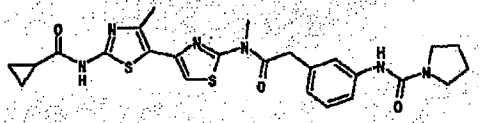
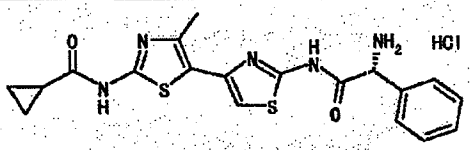
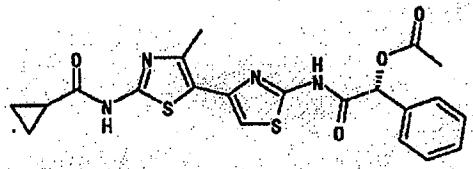
表 48

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
189	 C25H28N6O4S2	>90 結晶 221.8 – 223.3	DMSO-d6-300 0.89-0.9(m, 4H), 1.93(br, 1H), 2.48(s, 3H), 3.29-3.31(m, 4H), 3.58-3.6(m, 4H), 3.73(s, 3H), 4.07(s, 2H), 6.84(d, 1H, J=7.68Hz), 7.13(dd, 1H, J=7.88, 7.84Hz), 7.25(s, 1H), 7.43-7.47(m, 2H), 8.52(s, 1H), 12.33(s, 1H)	ESI+ 541(100)
190	 C29H29N5O4S2	>90 アモルファス	DMSO-d6-300 0.85-0.96(m, 4H), 1.88-1.97(m, 1H), 2.48(s, 3H), 3.33(s, 3H), 3.75(t, 2H, J=5.35Hz), 4.22(s, 2H), 4.47(t, 2H, J=5.35Hz), 7.01(d, 1H, J=7.7Hz), 7.28(s, 1H), 7.34(t, 1H, J=7.7Hz), 7.51-7.63(m, 3H), 7.71(s, 1H), 7.73(d, 1H, J=7.7Hz), 7.96(d, 2H, J=8.4Hz), 10	ESI+ 576(100)
191	 C30H31N5O4S2	>90 アモルファス	DMSO-d6-300 0.84-0.96(m, 4H), 1.88-2.08(m, 3H), 2.49(s, 3H), 3.31(s, 3H), 3.45(t, 2H, J=5.9Hz), 4.16(s, 2H), 4.30(t, 2H, J=5.9Hz), 7.05(d, 1H, J=8.0Hz), 7.26(s, 1H), 7.35(t, 1H, J=8.0Hz), 7.51~7.61(m, 3H), 7.74(d, 1H, J=8.0Hz), 7.75(s, 1H), 7.96(d, 2H, J=8.5Hz), 10.2	ESI+ 590(100)
192	 C26H25N5O4S2	>90 結晶 >155 dec.	DMSO-d6-300 2.14(s, 3H), 2.47(s, 3H), 3.65(q, 2H, J=5.5Hz), 4.28(s, 2H), 4.36(t, 2H, J=5.5Hz), 5.17(t, 1H, J=5.5Hz), 7.02(d, 1H, J=7.9Hz), 7.28(s, 1H), 7.34(t, 1H, J=7.9Hz), 7.51-7.63(m, 3H), 7.72(s, 1H), 7.73(d, 1H, J=7.9Hz), 7.97(d, 2H, J=8.8Hz), 10.28(s, 1H), 12.0	ESI+ 536(100)

[0136]

[Table 50]

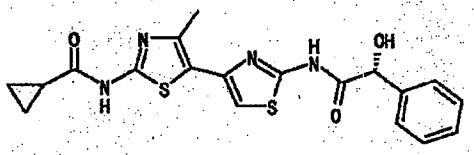
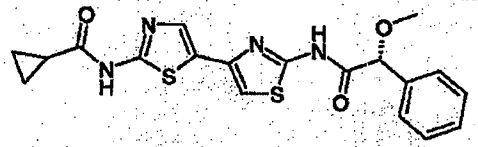
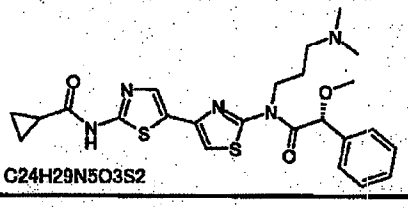
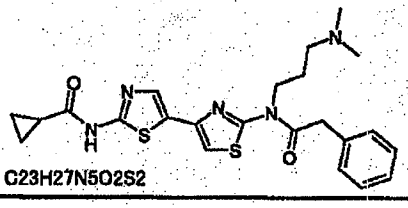
表 49

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
193	 C25H28N6O3S2	>90 結晶 >220	DMSO-d6-400 0.89-0.9(m, 4H), 1.84(br, 4H), 1.93(br, 1H), 2.48(s, 3H), 3.35(br, 4H), 3.73(s, 3H), 4.06(s, 2H), 6.84(d, 1H, J=7.68Hz), 7.13(dd, 1H, J=7.88, 7.84Hz), 7.25(s, 1H), 7.43-7.47(m, 2H), 8.09(s, 1H), 12.31(s, 1H)	ESI+ 525(100)
194	 C27H25N5O3S2	>90 アモルファス	DMSO-d6-400 0.89-0.9(m, 4H), 1.93(br, 1H), 2.47(s, 3H), 3.36(s, 3H), 3.66(s, 2H), 7.01-7.23(m, 10H), 12.31(br, 1H)	ESI+ 532(100)
195	 C19H20ClN5O2S2	>90 結晶 214.3 - 215.8	DMSO-d6-400 0.89-0.9(m, 4H), 1.93(br, 1H), 2.45(s, 3H), 5.28(br, 1H), 7.30(s, 1H), 7.47-7.6(m, 5H), 8.91(br, 1H), 12.31(s, 1H), 13.01(s, 1H)	ESI+ 414(100)
196	 C21H20N4O4S2	>90 アモルファス	DMSO-d6-400 0.89-0.9(m, 4H), 1.93(br, 1H), 2.16(s, 3H), 2.45(s, 3H), 5.09(s, 1H), 7.23(s, 1H), 7.42-7.44(m, 3H), 7.54-7.56(m, 2H), 12.29(s, 1H), 12.82(s, 1H)	ESI+ 457(100)

[0137]

[Table 51]

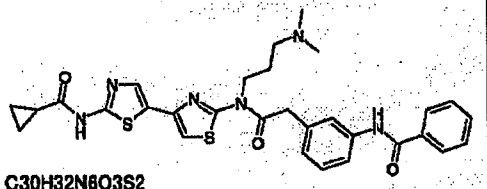
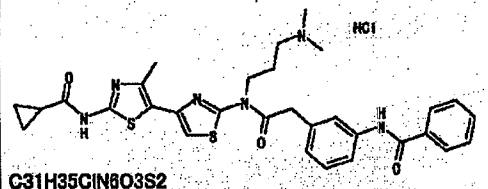
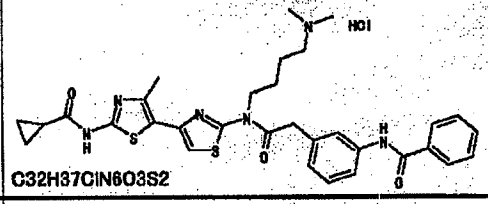
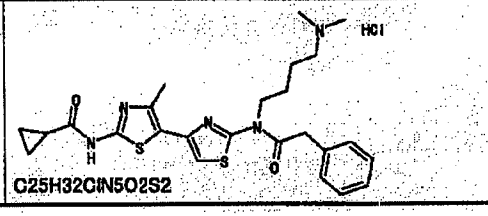
表 50

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
197	 C19H18N4O3S2	>90 結晶 >220	DMSO-d6-300 0.89-0.9(m, 4H), 1.93(br, 1H), 2.46(s, 3H), 5.28(br, 1H), 6.26(br, 1H), 7.2(s, 1H), 7.38-7.4(m, 3H), 7.51-7.53(m, 2H), 12.29(s, 1H), 12.44(s, 1H)	ESI+ 415(100)
198	 C19H18N4O3S2	>90 アモルファス	DMSO-d6-300 0.85-0.98(m, 4H), 1.91-2.02(m, 1H), 3.34(s, 3H), 5.06(s, 1H), 7.33-7.53(m, 6H), 7.83(s, 1H), 12.43(s, 1H), 12.61(s, 1H)	ESI+ 415(100)
199	 C24H29N5O3S2	>90 アモルファス	DMSO-d6-300 0.85-0.97(m, 4H), 1.42-1.54(m, 1H), 1.72-1.84(m, 1H), 1.91-1.99(m, 1H), 2.15(s, 6H), 2.19-2.29(m, 2H), 3.36(s, 3H), 3.99-4.21(m, 2H), 5.60(s, 1H), 7.35-7.49(m, 5H), 7.52(s, 1H), 7.84(s, 1H), 12.42(s, 1H)	ESI+ 500(100)
200	 C23H27N5O2S2	>90 結晶 198.2-200.2 dec.	DMSO-d6-300 0.86-0.97(m, 4H), 1.79-2.01(m, 3H), 2.18(s, 6H), 2.25-2.38(m, 2H), 4.18(s, 2H), 4.21-4.31(m, 2H), 7.25-7.39(m, 5H), 7.46(s, 1H), 7.84(s, 1H), 12.42(s, 1H)	ESI+ 470(100)

[0138]

[Table 52]

表 51

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
201	 C30H32N6O3S2	>90 結晶 215.1 - 217.5	DMSO-d6-400 0.87-0.96(m, 4H), 1.83-2(m, 3H), 2.18(s, 6H), 2.28-2.36(m, 2H), 4.19(s, 2H), 4.21-4.3(m, 2H), 7.04(d, 1H, J=7.9Hz), 7.33(t, 1H, J=7.9Hz), 7.46(s, 1H), 7.50(s, 3H), 7.72(d, 1H, J=7.9Hz), 7.74(s, 1H), 7.83(s, 1H), 7.95(d, 2H, J=7.4Hz), 10.25(s, 1H), 12.38(s	ESI+ 589(100)
202	 C31H35ClN6O3S2	>90 結晶 157 - 162	DMSO-d6-300 0.88-0.91(m, 4H), 1.75-2(m, 1H), 2.18(br, 2H), 2.49(br, 3H), 2.76(s, 3H), 2.78(s, 3H), 3.2(br, 2H), 4.18(br, 2H), 4.3(br, 2H), 7.09(d, 1H, J=9Hz), 7.29-7.37(m, 2H), 7.52-7.59(m, 3H), 7.69(d, 1H, J=9Hz), 7.8(s, 1H), 7.96(d, 2H, J=6Hz), 10.32(br, 1H)	ESI+ 603(100)
203	 C32H37ClN6O3S2	>90 結晶 210 - 215	DMSO-d6-300 0.88-0.92(m, 4H), 1.85-2.0(m, 4H), 1.95-2(m, 1H), 2.73(s, 3H), 2.75(s, 3H), 3.09(br, 2H), 4.17(s, 2H), 4.26(br, 2H), 7.08(d, 1H, J=6Hz), 7.28(s, 1H), 7.35(t, 1H, J=7.5Hz), 7.5-7.59(m, 3H), 7.7(d, 1H, J=8Hz), 7.79(s, 1H), 7.97(d, 2H, J=9Hz), 10.15(br, 1H), 10.32(s, 1H)	ESI+ 617(100)
204	 C25H32ClN5O2S2	>90 結晶 188 - 191	DMSO-d6-300 0.87-0.93(m, 4H), 1.78(br, 4H), 1.95-2(m, 1H), 2.53(s, 3H), 2.73(s, 3H), 2.75(s, 3H), 3.09(br, 2H), 4.17(s, 2H), 4.25(br, 2H), 7.26(s, 1H), 7.28-7.39(m, 5H)	ESI+ 498(100)

[0139]

[Table 53]

表 52

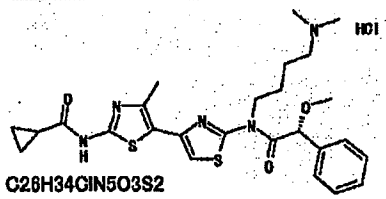
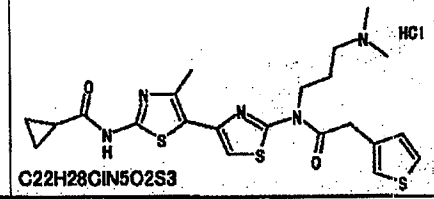
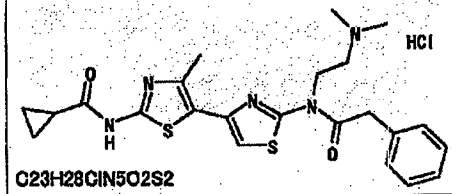
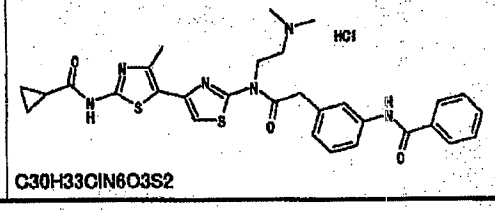
実施例番号	構造式 ／ 組成式	純度 ／性状／ 融点 (%) (℃)	1H NMR(δ)ppm	MS
205	 C26H34ClN5O3S2	>90 結晶 167 - 169	DMSO-d6-300 0.86-0.92(m, 4H), 1.68(br, 2H), 1.95-2(m, 1H), 2.49(s, 3H), 2.71(s, 3H), 2.73(s, 3H), 3.37(s, 3H), 3.9(br, 2H), 4.06(br, 2H), 5.59(s, 1H), 7.32(s, 1H), 7.4-7.46(m, 5H)	ESI+ 528(100)
206	 C22H28ClN5O2S3	>90 結晶 >250	DMSO-d6-300 0.88-0.93(m, 4H), 1.95-2.0(br, 1H), 2.27(br, 2H), 2.5(s, 3H), 2.75(s, 3H), 2.77(s, 3H), 3.18(br, 2H), 4.18(s, 2H), 4.29(br, 2H), 7.11(d, 1H, J=9Hz), 7.28(s, 1H), 7.43(br, 1H), 7.53(br, 1H)	ESI+ 490(100)
207	 C23H28ClN5O2S2	>90 結晶 >250	DMSO-d6-300 0.88-0.93(m, 4H), 1.93-5-2.0(br, 1H), 2.46(s, 3H), 2.91(s, 3H), 2.92(s, 3H), 3.5(br, 2H), 4.22(s, 2H), 4.65(br, 2H), 7.3(s, 1H), 7.36-7.37(m, 5H)	ESI+ 470(100)
208	 C30H33ClN6O3S2	>90 結晶 194.5 - 198	DMSO-d6-300 0.88-0.93(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 2.92(s, 3H), 2.93(s, 3H), 3.5(br, 2H), 4.24(s, 2H), 4.66(br, 2H), 7.12(d, 1H, J=6Hz), 7.32-7.37(m, 2H), 7.36-7.37(m, 3H), 7.69(d, 1H, J=9Hz), 7.81(s, 1H), 7.97(d, 2H, J=6Hz)	ESI+ 589(100)

表 54

実施例番号	構造式／組成式	純度（%）／性状／融点（℃）	1H NMR(δ)ppm	MS
213	C21H22BrN5O2S2	>90 結晶 >220	DMSO-d6-300 0.88-1.00(m, 4H), 1.91-2.00(m, 1H), 2.46(s, 3H), 3.71-3.84(m, 2H), 4.43-4.59(m, 2H), 5.69(s, 1H), 7.44(s, 1H), 7.48-7.61(m, 5H), 9.81(br, 2H), 12.42(s, 1H)	ESI+ 440(100)
214	C26H31ClN8O2S2	>90 結晶 132 - 137	DMSO-d6-300 0.87-0.98(m, 4H), 1.94-1.98(m, 1H), 2.05-2.15(m, 2H), 2.5(s, 3H), 2.72(s, 3H), 2.74(s, 3H), 3.13-3.2(m, 2H), 4.22(s, 2H), 4.3-4.35(m, 2H), 7(t, 1H, J=6.75Hz), 7.1(t, 1H, J=7.5Hz), , 7.26(s, 1H), 7.37-7.39(m, 2H), 7.58(d, 1H, J=9Hz)	ESI+ 523(100)
215	C25H32ClN5O2S2	>90 アモルファス	DMSO-d6-400 0.89-0.9(m, 4H), 1.32(t, 6H, J=7.22Hz), 1.93(br, 1H), 2.47(s, 3H), 3.32(br, 4H), 3.44(br, 2H), 4.23(s, 2H), 4.62(br, 2H), 7.3-7.37(m, 6H), 7.51-7.53(m, 2H), 10.59(br, 1H), 12.34(s, 1H)	ESI+ 498(100)
216	C26H32ClN5O2S2	>90 結晶 >220	DMSO-d6-400 0.89-0.9(m, 4H), 1.42(br, 1H), 1.69-1.93(br, 6H), 2.48(s, 3H), 3.08(br, 2H), 3.44(br, 2H), 3.65(br, 2H), 4.22(s, 2H), 4.71(br, 2H), 7.31-7.37(m, 6H), 7.51-7.53(m, 2H), 10.28(br, 1H), 12.34(s, 1H)	ESI+ 510(100)

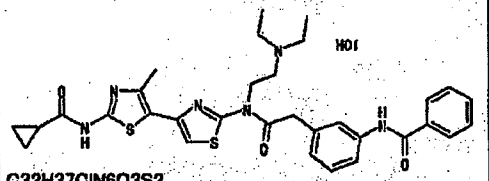
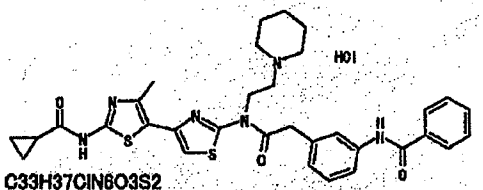
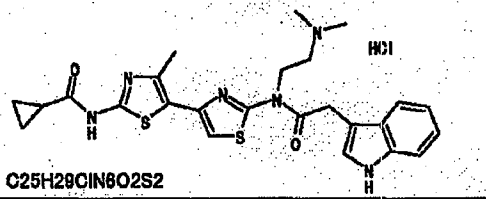
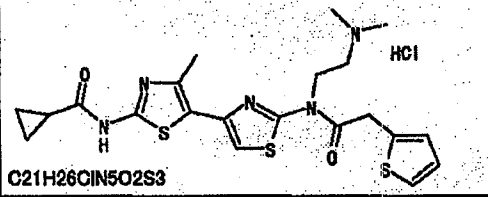
[0141]

[Table 55]

[0142]

[Table 56]

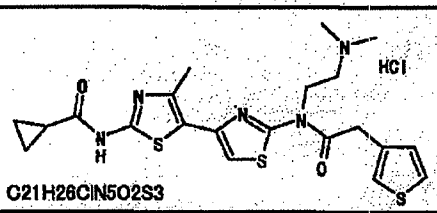
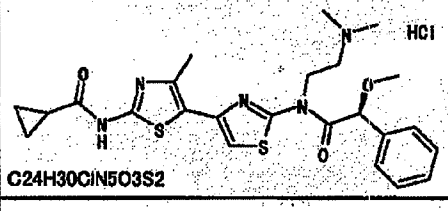
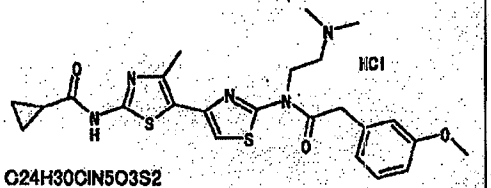
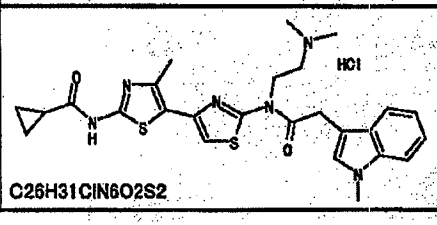
表 55

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
217	 C32H37ClN6O3S2	>90 結晶 212.3 - 214.3	DMSO-d6-400 0.89-0.9(m, 4H), 1.32(t, 6H, J=7.22Hz), 1.93(br, 1H), 2.47(s, 3H), 3.32(br, 4H), 4.24(s, 2H), 4.69(br, 2H), 7.09(d, 1H, J=7.68Hz), 7.33-7.37(m, 2H), 7.53-7.68(m, 5H), 7.82(s, 1H), 7.96(d, 2H, J=7.08Hz), 10.28(s, 1H), 12.34(s, 1H)	ESI+ 617(100)
218	 C33H37ClN6O3S2	>90 アモルファス	DMSO-d6-400 0.89-0.9(m, 4H), 1.42(br, 1H), 1.69-1.93(br, 6H), 2.48(s, 3H), 3.08(br, 2H), 3.49(br, 2H), 3.59(br, 2H), 4.23(s, 2H), 4.71(br, 2H), 7.09(d, 1H, J=7.68Hz), 7.32-7.37(m, 2H), 7.52-7.67(m, 5H), 7.83(s, 1H), 7.96(d, 2H, J=7.08Hz), 10.28(s, 1H), 12.35(s, 1H)	ESI+ 628(100)
219	 C25H29ClN6O2S2	>90 結晶 189 - 191	DMSO-d6-300 0.88-0.98(m, 4H), 1.93-1.98(m, 1H), 2.48(s, 3H), 2.9(s, 3H), 2.91(s, 3H), 3.45(br, 2H), 4.26(s, 2H), 4.7(br, 2H), 6.99(t, 1H, J=7.5Hz), 7.09(t, 1H, J=8Hz), 7.28(s, 1H), 7.38(d, 1H, J=9Hz), 7.52(s, 1H), 7.61(d, 1H, J=9Hz)	ESI+ 509(100)
220	 C21H26ClN5O2S3	>90 結晶 147 - 151	DMSO-d6-300 0.88-0.98(m, 4H), 1.93-1.98(m, 1H), 2.45(s, 3H), 2.91(s, 3H), 2.92(s, 3H), 3.5(br, 2H), 4.5(s, 2H), 4.65(br, 2H), 7.03(d, 1H, J=6Hz), 7.11(s, 1H), 7.32(s, 1H), 7.48(d, 1H, J=3Hz)	ESI+ 476(100)

[0143]

[Table 57]

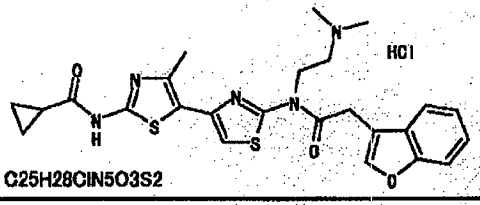
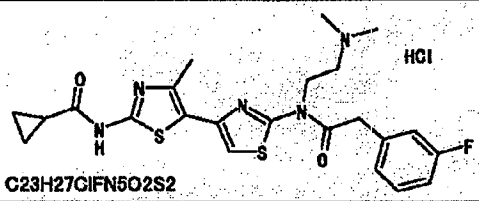
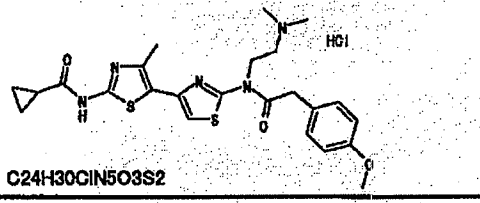
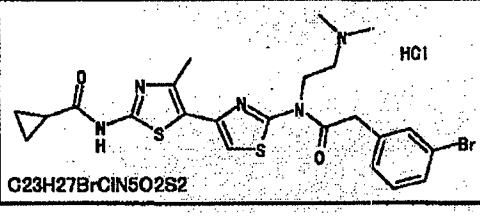
表 56

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
221	 C21H26ClN5O2S3	>90 結晶 150 - 155	DMSO-d6-300 0.85-0.95(m, 4H), 1.9-2(m, 1H), 2.49(s, 3H), 2.9(s, 3H), 2.92(s, 3H), 3.46(br, 2H), 4.3(s, 2H), 4.65(br, 2H), 7.12(d, 1H, J=6Hz), 7.31(s, 1H), 7.49-7.54(m, 2H)	ESI+ 476(100)
222	 C24H30ClN5O3S2	>90 結晶 96 - 99	DMSO-d6-300 0.85-0.95(m, 4H), 1.93-1.98(m, 1H), 2.49(s, 3H), 2.87(s, 3H), 2.89(s, 3H), 3.15-3.3(m, 2H), 3.36(s, 3H), 4.5-4.6(m, 2H), 5.72(s, 1H), 7.36(s, 1H), 7.42-7.45(m, 3H), 7.54-7.58(m, 2H)	ESI+ 500(100)
223	 C24H30ClN5O3S2	>90 結晶 218 - 222	DMSO-d6-300 0.85-0.95(m, 4H), 1.93-1.98(m, 1H), 2.49(s, 3H), 2.9(s, 3H), 2.92(s, 3H), 3.49(br, 2H), 3.73(s, 3H), 4.18(s, 2H), 4.64(br, 2H), 6.85-6.97(m, 3H), 7.24-7.31(m, 2H)	ESI+ 500(100)
224	 C26H31ClN6O2S2	>90 結晶 188 - 190	DMSO-d6-300 0.85-0.95(m, 4H), 1.93-1.98(m, 1H), 2.49(s, 3H), 2.9(s, 3H), 2.92(s, 3H), 3.48(br, 2H), 3.78(s, 3H), 4.27(s, 2H), 4.65-4.65(m, 2H), 7.04(t, 1H, J=7.5Hz), 7.17(t, 1H, J=7.5Hz), 7.29(s, 1H), 7.41-7.46(m, 2H), 7.62(d, 1H, J=6Hz)	ESI+ 523(100)

[0144]

[Table 58]

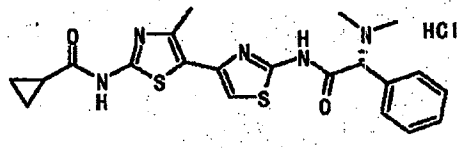
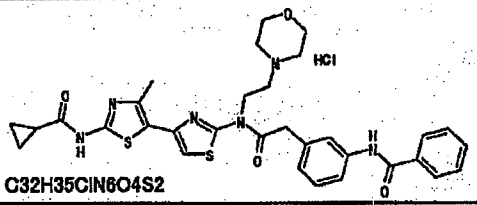
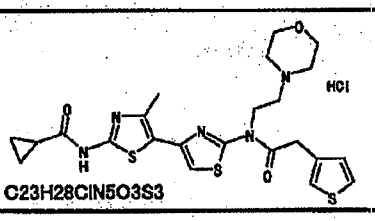
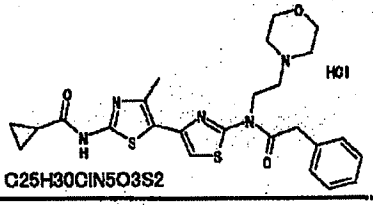
表 57

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
225	 C25H28ClN5O3S2	>90 結晶 >250	DMSO-d6-300 0.85-0.95(m, 4H), 1.93-1.96(m, 1H), 2.49(s, 3H), 2.94(s, 3H), 2.95(s, 3H), 3.58(br, 2H), 4.36(s, 2H), 4.7-4.75(m, 2H), 7.26-7.36(m, 3H), 7.59(d, 1H, J=8Hz), 7.71(d, 1H, J=9Hz), 8.06(s, 1H)	ESI+ 510(100)
226	 C23H27ClFN5O2S2	>90 結晶 248 - 251	DMSO-d6-300 0.85-0.95(m, 4H), 1.93-1.96(m, 1H), 2.49(s, 3H), 2.92(s, 3H), 2.94(s, 3H), 3.54(br, 2H), 4.26(s, 2H), 4.6-4.7(m, 2H), 7.14-7.21(m, 2H), 7.31(s, 1H), 7.39-7.42(m, 2H)	ESI+ 488(100)
227	 C24H30ClN5O3S2	>90 結晶 214 - 219	DMSO-d6-300 0.85-0.95(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 2.91(s, 3H), 2.93(s, 3H), 3.49(br, 2H), 3.75(s, 3H), 4.14(s, 2H), 4.62-4.66(m, 2H), 6.92(d, 2H, J=9Hz), 7.27-7.3(m, 3H)	ESI+ 500(100)
228	 C23H27BrClN5O2S2	>90 結晶 198 - 201	DMSO-d6-300 0.85-0.95(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 2.92(s, 3H), 2.94(s, 3H), 3.54(br, 2H), 4.28(s, 2H), 4.64-4.68(m, 2H), 7.31-7.35(m, 3H), 7.49-7.51(m, 1H), 7.8(s, 1H)	ESI+ 548(100)

[0145]

[Table 59]

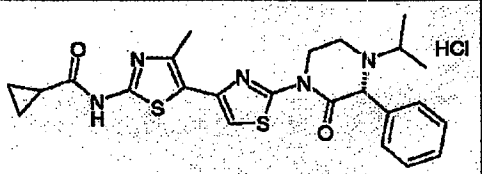
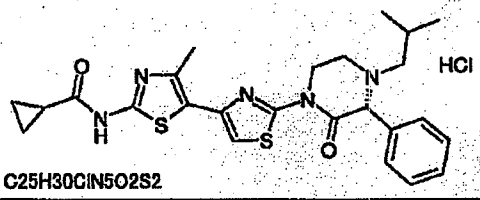
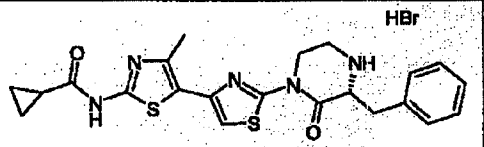
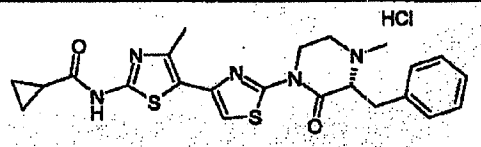
表 58

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
229	 C21H24ClN5O2S2	>90 結晶 >220	DMSO-d6-300 0.89-0.9(m, 4H), 1.93(br, 1H), 2.45(s, 3H), 2.99(br, 2H), 4.71(br, 1H), 7.34(s, 1H), 7.52-7.62(m, 5H), 10.83(br, 1H), 12.35(s, 1H), 12.69(s, 1H)	ESI+ 442(100)
230	 C32H35ClN6O4S2	>90 結晶 >220	DMSO-d6-300 0.85-0.95(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 3.29(br, 2H), 3.54(br, 2H), 3.6-3.7(m, 2H), 3.8-3.9(m, 2H), 4.01-4.06(m, 2H), 4.24(s, 2H), 4.65-4.73(m, 2H), 7.13(d, 1H, J=9Hz), 7.32-7.37(m, 2H), 7.5-7.67(m, 3H), 7.76(d, 1H, J=33Hz), 7.81(s, 1H), 7.97(d, 2H, J=9Hz)	ESI+ 631(100)
231	 C23H28ClN5O3S3	>90 結晶 >230	DMSO-d6-300 0.85-0.95(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 3.26(br, 2H), 3.51(br, 2H), 3.62-3.66(m, 2H), 3.8-3.9(m, 2H), 4.01-4.1(m, 2H), 4.24(s, 2H), 4.65-4.75(m, 2H), 7.11-7.14(m, 1H), 7.31(s, 1H), 7.52-7.54(m, 2H)	ESI+ 518(100)
232	 C25H30ClN5O3S2	>90 結晶 >230	DMSO-d6-300 0.89-0.93(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 3.25-3.3(m, 2H), 3.52-3.56(m, 2H), 3.63-3.68(m, 2H), 3.83-3.88(m, 2H), 4-4.05(m, 2H), 4.23(s, 2H), 4.68-4.72(m, 2H), 7.31-7.38(m, 6H)	ESI+ 512(100)

[0146]

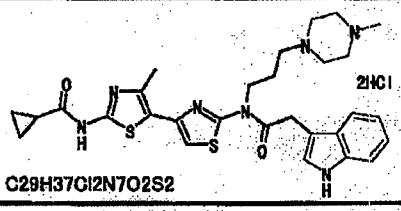
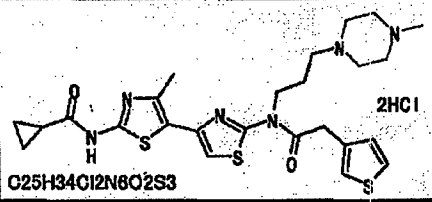
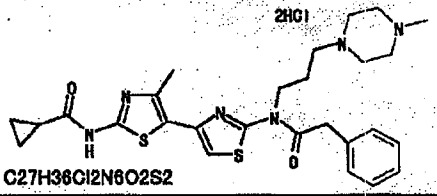
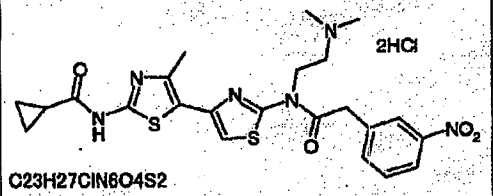
[Table 60]

表 59

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
233	 HCl C24H28ClN5O2S2	>90 アモルファス	DMSO-d6-300 0.91-1.32(m, 10H), 1.88-2.01(m, 1H), 2.46(s, 3H), 3.91-4.21(m, 4H), 4.55(br, 1H), 7.21-7.62(m, 6H), 12.39(s, 1H)	ESI+ 482(100)
234	 HCl C25H30ClN5O2S2	>90 アモルファス	DMSO-d6-300 0.91-1.32(m, 10H), 1.88-2.01(m, 1H), 2.46(s, 3H), 3.91-4.21(m, 4H), 4.55(br, 1H), 7.21-7.62(m, 6H), 12.39(s, 1H)	ESI+ 482(100)
235	 HBr C22H24BrN5O2S2	>90 結晶 >220	DMSO-d6-300 0.84-0.99(m, 4H), 1.90-1.99(m, 1H), 2.47(s, 3H), 3.18(dd, 1H, J=8.4, 14.7Hz), 3.56(dd, 1H, J=5.1, 14.6Hz), 3.53-3.73(m, 2H), 4.24-4.35(m, 1H), 4.44-4.55(m, 1H), 4.70(br, 1H), 7.29-7.47(m, 6H), 9.40(br, 1H), 9.61(br, 1H), 12.41(s, 1H)	
236	 HCl C23H26ClN5O2S2	>90 アモルファス	DMSO-d6-300 0.85-0.95(m, 4H), 1.89-1.99(m, 1H), 2.49(s, 3H), 2.72-2.94(m, 2H), 3.33-3.44(m, 2H), 3.87-4.08(m, 2H), 4.36-4.52(m, 1H), 7.18-7.42(m, 6H), 12.40(s, 1H)	ESI+ 468(100)

[0147]
[Table 61]

表 60

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
237	 C29H37Cl2N7O2S2	>90 結晶 110 - 118	DMSO-d6-300 0.85-0.95(m, 4H), 1.94-1.98(m, 1H), 2.21(br, 2H), 2.49(s, 3H), 2.82(s, 3H), 3.35(br, 2H), 3.35-3.35(m, 4H), 3.65-3.75(m, 4H), 4.23(s, 2H), 4.34-4.38(m, 2H), 6.8-7.02(m, 1H), 7.07-7.09(m, 1H), 7.27(s, 1H), 7.27-7.37(m, 2H), 7.58(d, 1H, J=6Hz)	ESI+ 578(100)
238	 C25H34Cl2N6O2S3	>90 結晶 193.5 - 195	DMSO-d6-300 0.85-0.95(m, 4H), 1.94-1.98(m, 1H), 2.23(br, 2H), 2.82(s, 3H), 3.3-3.35(m, 2H), 3.4-3.45(m, 4H), 3.65-3.65(m, 4H), 4.19(s, 2H), 4.3-4.35(m, 2H), 7.08(d, 1H, J=6Hz), 7.29(s, 1H), 7.43(s, 1H), 7.51-7.54(m, 1H)	ESI+ 545(100)
239	 C27H36Cl2N6O2S2	>90 結晶 115 - 120	DMSO-d6-300 0.85-0.95(m, 4H), 1.94-1.98(m, 1H), 2.27(br, 2H), 2.5(s, 3H), 2.82(s,3H), 3.2-3.35(m, 2H), 3.34-3.5(m, 4H), 3.65-3.7(m, 4H), 4.18(s, 2H), 4.3-4.4(m, 2H), 7.29-7.36(m, 6H)	ESI+ 539(100)
240	 C23H27ClN6O4S2	>90 アモルファス	DMSO-d6-300 0.83-0.95(m, 4H), 1.87-2.01(m, 1H), 2.48(s, 3H), 2.96(s, 3H), 2.97(s, 3H), 3.55-3.64(m, 2H), 4.43(s, 2H), 4.60-4.71(m, 2H), 7.32(s, 1H), 7.69(t, 1H, J=7.9Hz), 7.81(d, 1H, J=8.1Hz), 8.19(d, 1H, J=8.1Hz), 8.30(s, 1H), 10.44(br, 1H), 12.40(s, 1H)	ESI+ 515(100)

[0148]

[Table 62]

表 61

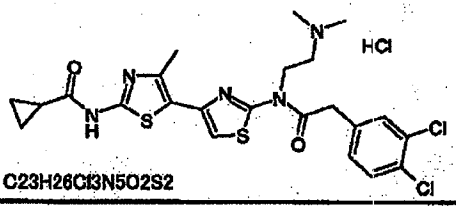
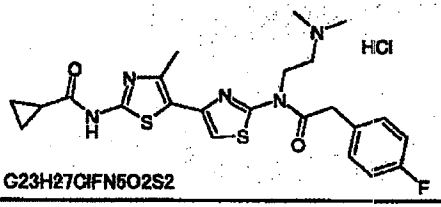
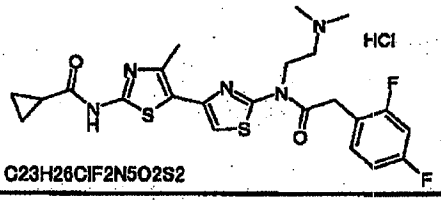
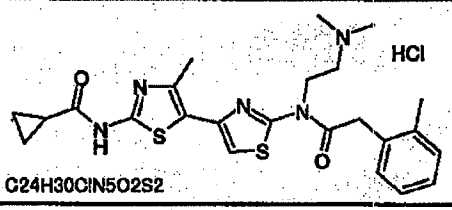
実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
241	 C23H26Cl3N5O2S2	>90 アモルファス	DMSO-d6-300 0.86-0.97(m, 4H), 1.90-2.00(m, 1H), 2.47(s, 3H), 2.95(s, 3H), 2.96(s, 3H), 3.52-3.63(m, 2H), 4.28(s, 2H), 4.60-4.70(m, 2H), 7.33(s, 1H), 7.37(d, 1H, J=8.4Hz), 7.66(d, 1H, J=8.4Hz), 7.68(s, 1H), 10.57(br, 1H), 12.41(s, 1H)	ESI+ 538(100)
242	 C23H27ClFN5O2S2	>90 アモルファス	DMSO-d6-300 0.84-0.97(m, 4H), 1.90-1.98(m, 1H), 2.50(s, 3H), 2.95(s, 3H), 2.97(s, 3H), 3.50-3.59(m, 2H), 4.22(s, 2H), 4.61-4.68(m, 2H), 7.18-7.43(m, 5H), 10.37(br, 1H), 12.40(s, 1H)	ESI+ 488(100)
243	 C23H26ClF2N5O2S2	>90 結晶 >220	DMSO-d6-300 0.86-0.98(m, 4H), 1.9-1.98(m, 1H), 2.48(s, 3H), 2.96(s, 3H), 2.98(s, 3H), 3.54-3.63(m, 2H), 4.28(s, 2H), 4.64-4.75(m, 2H), 7.09-7.51(m, 4H), 10.32(br, 1H), 12.4(s, 1H)	ESI+ 506(100)
244	 C24H30ClN5O2S2	>90 結晶 >220	DMSO-d6-300 0.85-0.97(m, 4H), 1.90-2.01(m, 1H), 2.22(s, 3H), 2.48(s, 3H), 2.95(s, 3H), 2.97(s, 3H), 3.50-3.60(m, 2H), 4.22(s, 2H), 4.61-4.74(m, 2H), 7.17-7.26(m, 4H), 7.33(s, 1H), 10.50(br, 1H), 12.41(s, 1H)	ESI+ 484(100)

表 62

実施例番号	構造式 ／ 組成式	純度（%）／性状 ／ 融点（℃）	1H NMR(δ)ppm	MS
245	 C24H30ClN5O2S2	>90 アモルファス	DMSO-d6-300 0.84-0.96(m, 4H), 1.90-1.99(m, 1H), 2.31(s, 3H), 2.48(s, 3H), 2.93(s, 3H), 2.95(s, 3H), 3.44-3.53(m, 2H), 4.15(s, 2H), 4.57-4.66(m, 2H), 7.18(d, 2H, J=8.1Hz), 7.24(d, 2H, J=8.1Hz), 7.32(s, 1H), 10.38(br, 1H), 12.40(s, 1H)	ESI+ 484(100)
246	 C23H27Cl2N5O2S2	>90 結晶 >220	DMSO-d6-300 0.86-0.96(m, 4H), 1.85-1.99(m, 1H), 2.47(s, 3H), 2.92(s, 3H), 2.98(s, 3H), 3.44-3.56(m, 2H), 4.15(s, 2H), 4.55-4.66(m, 2H), 7.26-7.47(m, 5H), 10.31(br, 1H), 12.38(s, 1H)	ESI+ 504(100)
247	 C24H27ClF3N5O2S2	>90 結晶 >220	DMSO-d6-300 0.86-0.96(m, 4H), 1.85-1.99(m, 1H), 2.47(s, 3H), 2.95(s, 3H), 2.97(s, 3H), 3.53-3.65(m, 2H), 4.37(s, 2H), 4.61-4.75(m, 2H), 7.32(s, 1H), 7.59-7.69(m, 3H), 7.75(2, 1H), 10.61(br, 1H), 12.39(s, 1H)	ESI+ 538(100)
248	 C23H26ClF2N5O2S2	>90 結晶 >220	DMSO-d6-300 0.86-0.96(m, 4H), 1.90-1.99(m, 1H), 2.47(s, 3H), 2.95(s, 3H), 2.96(s, 3H), 3.53-3.65(m, 2H), 4.29(s, 2H), 4.57-4.66(m, 2H), 7.10-7.21(m, 3H), 7.22(s, 1H), 10.51(br, 1H), 12.39(s, 1H)	ESI+ 506(100)

[0149]

[Table 63]

表 63

実施例番号	構造式 / 組成式	純度 (%)	性状 / 融点 (℃)	1H NMR(δ)ppm	MS
249	C24H28ClN5O2S2	>90	結晶 >220	DMSO-d6-300 0.89-0.9(m, 4H), 1.46(br, 1H), 1.81(br, 6H), 2.45(s, 3H), 2.85(br, 2H), 3.12(br, 1H), 3.52(br, 1H), 5.35(br, 1H), 7.33(s, 1H), 7.52-7.63(m, 5H), 10.46(br, 1H), 12.28(s, 1H), 13.28(s, 1H)	ESI+ 482(100)
250	C25H30ClN5O2S2	>90	結晶 >220	DMSO-d6-300 0.89-0.9(m, 4H), 1.92(br, 5H), 3.21(br, 3H), 2.47(s, 3H), 3.27(br, 1H), 4.2(s, 1H), 4.3(br, 1H), 4.63(br, 1H), 7.07(s, 1H), 7.25-7.39(m, 5H)	ESI+ 496(100)
251	C32H35ClN6O3S2	>90	アモルファス	DMSO-d6-400 0.89-0.9(m, 4H), 1.92(br, 5H), 3.21(br, 3H), 2.47(s, 3H), 3.27(br, 1H), 4.2(s, 1H), 4.3(br, 1H), 4.63(br, 1H), 7.07-7.13(m, 2Hx1/2), 7.15(s, 1H), 7.25-7.39(m, 2Hx1/2), 7.51-7.63(m, 10Hx1/2), 7.82(s, 2Hx1/2), 7.85-7.97(m, 4Hx1/2), 10.23(s, 1Hx1/2), 10.28(s	ESI+ 615(100)
252	C23H26Cl3N5O2S2	>90	結晶 >220	DMSO-d6-300 0.89-0.9(m, 4H), 1.93(br, 1H), 2.51(s, 3H), 2.97(s, 3H), 2.99(s, 3H), 3.62(br, 2H), 4.54(s, 2H), 4.81(br, 2H), 7.35(s, 1H), 7.41-7.44(m, 1H), 7.55(d, 2H, J=8.43Hz), 10.28(s, 1H), 12.34(s, 1H)	ESI+ 538(100), 540(100)

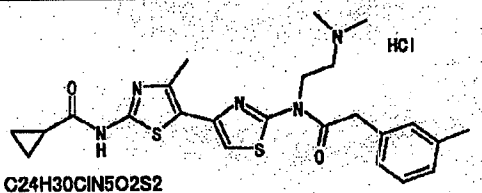
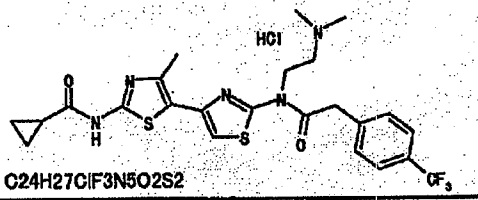
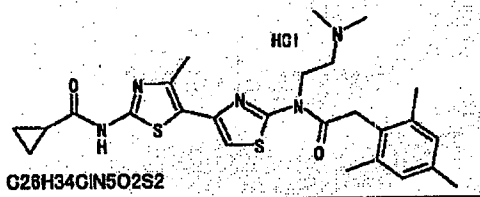
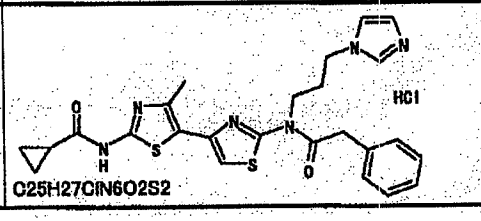
[0150]

[Table 64]

[0151]

[Table 65]

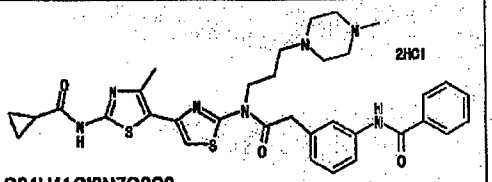
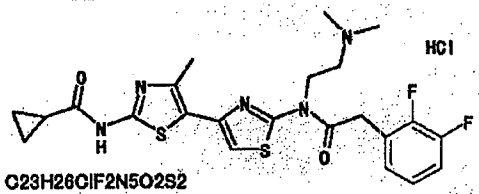
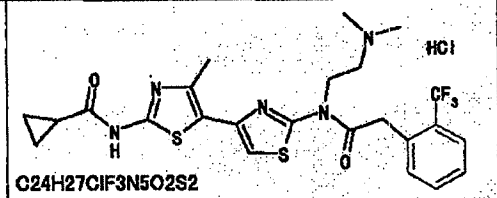
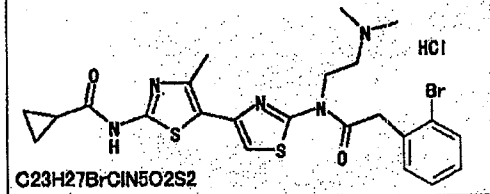
表 64

実施例番号	構造式 / 組成式	純度 (%) / 性状 / 融点 (℃)	1H NMR(δ)ppm	MS
253	 C24H30ClN5O2S2	>90 結晶 >220	DMSO-d6-400 0.89-0.9(m, 4H), 1.93(br, 1H), 2.31(s, 3H), 2.92(s, 3H), 2.94(s, 3H), 3.51(br, 2H), 4.15(s, 2H), 4.63(br, 2H), 7.11-7.16(m, 3H), 7.24-7.26(m, 1H), 7.3(s, 1H), 10.48(s, 1H), 12.36(s, 1H)	ESI+ 484(100)
254	 C24H27ClF3N5O2S2	>90 結晶 >220	DMSO-d6-300 0.89-0.9(m, 4H), 1.93(br, 1H), 2.31(s, 3H), 2.94(s, 3H), 2.96(s, 3H), 4.36(s, 2H), 4.63(br, 2H), 7.31(s, 1H), 7.58(br, 2H), 7.73(br, 2H), 10.55(br, 1H), 12.36(br, 1H)	ESI+ 538(100)
255	 C28H34ClN5O2S2	>90 結晶 >220	DMSO-d6-300 0.89-0.9(m, 4H), 1.93(br, 1H), 2.17(s, 6H), 2.23(s, 3H), 2.96(s, 3H), 2.98(s, 3H), 3.49(s, 2H), 4.63(br, 2H), 6.96(s, 1H), 7.39(s, 1H), 10.55(br, 1H), 12.36(br, 1H)	ESI+ 512(100)
256	 C25H27ClN6O2S2	>90 アモルファス	DMSO-d6-300 0.89-0.9(m, 4H), 1.93(br, 1H), 2.39(br, 2H), 2.45(s, 3H), 4.12(s, 2H), 4.45(br, 2H), 7.26-7.35(m, 6H), 7.75(s, 1H), 7.86(s, 1H), 9.18(s, 1H), 12.32(br, 1H)	ESI+ 507(100)

[0152]

[Table 66]

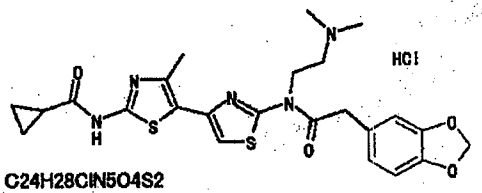
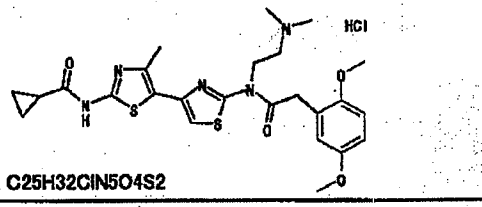
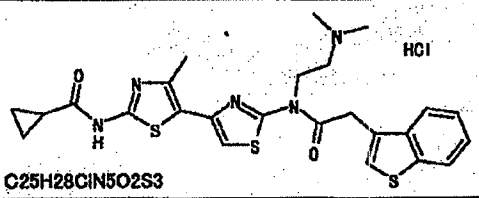
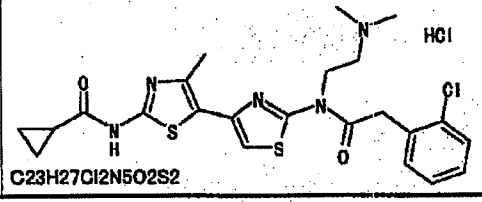
表 65

実施例番号	構造式 / 組成式	純度 (%) / 性状 / 融点 (℃)	1H NMR(δ)ppm	MS
257	 C34H41Cl2N7O3S2	>90 アモルファス 208.5 - 219.5	DMSO-d6-300 0.85-0.95(m, 4H), 1.94-1.98(m, 1H), 2.27(br, 2H), 2.5(s, 3H), 2.82(s, 3H), 3.2-3.34(m, 2H), 3.34-3.5(m, 4H), 3.65-3.7(m, 4H), 4.19(s, 2H), 4.3-4.35(m, 2H), 7.09(d, 1H, J=6Hz), 7.29-7.37(m, 2H), 7.5-7.68(m, 3H), 7.74(d, 1H, J=24Hz), 7.95(s, 1H), 7.97(d, 2H, J=9Hz)	ESI+ 658(100)
258	 C23H26ClF2N5O2S2	>90 結晶 >250	DMSO-d6-300 0.85-0.95(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 2.94(s, 3H), 2.95(s, 3H), 3.57(br, 2H), 4.39(s, 2H), 4.67-4.72(m, 2H), 7.22-7.23(m, 2H), 7.33(s, 1H), 7.34(s, 1H)	ESI+ 506(100)
259	 C24H27ClF3N5O2S2	>90 結晶 >250	DMSO-d6-300 0.85-0.95(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 2.94(s, 3H), 2.96(s, 3H), 3.53(br, 2H), 4.4(s, 2H), 4.72(br, 2H), 7.32(s, 1H), 7.55-7.58(m, 2H), 7.68-7.77(m, 2H)	ESI+ 538(100)
260	 C23H27BrClN5O2S2	>90 結晶 >250	DMSO-d6-300 0.85-0.95(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 2.95(s, 3H), 2.96(s, 3H), 3.57(br, 2H), 4.37(s, 2H), 4.7-4.75(m, 2H), 7.28-7.32(m, 2H), 7.41-7.47(m, 2H), 7.66(d, 1H, J=9Hz)	ESI+ 550(100)

[0153]

[Table 67]

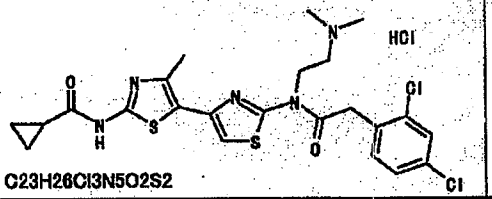
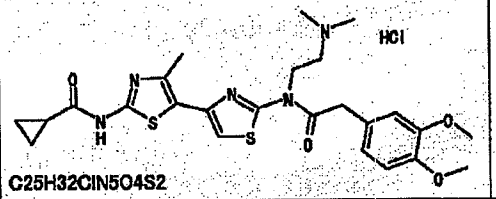
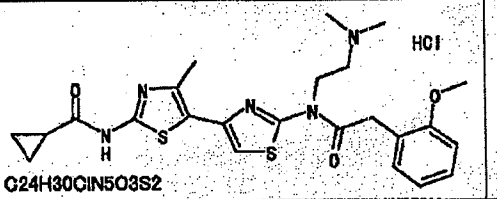
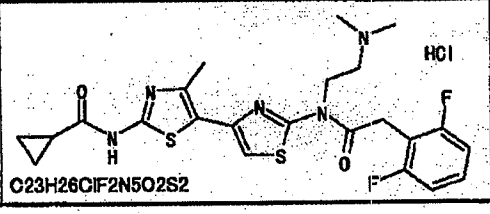
表 66

実施例番号	構造式 / 組成式	純度 (%) / 性状 / 融点 (°C)	1H NMR(δ)ppm	MS
261	 C24H28ClN5O4S2	>90 アモルファス >219 - 227	DMSO-d6-300 0.85-0.95(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 2.92(s, 3H), 2.93(s, 3H), 3.5(br, 2H), 4.12(s, 2H), 4.6-4.65(m, 2H), 6.01(s, 2H), 6.83-6.94(m, 3H), 7.31(s, 1H)	ESI+ 514(100)
262	 C25H32ClN5O4S2	>90 アモルファス 131 - 139	DMSO-d6-300 0.9-0.92(m, 4H), 1.94-1.98(m, 1H), 2.94(s, 3H), 2.93(s, 3H), 2.95(s, 3H), 3.48-3.52(m, 2H), 3.69(s, 3H), 3.71(s, 3H), 4.08(s, 2H), 4.69-4.72(m, 2H), 6.84-6.95(m, 3H), 7.3(s, 1H)	ESI+ 530(100)
263	 C25H28ClN5O2S3	>90 結晶 248 - 250.5	DMSO-d6-300 0.85-0.95(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 2.94(s, 3H), 2.96(s, 3H), 3.55-3.65(m, 2H), 4.51(s, 2H), 4.72-4.72(m, 2H), 7.31(s, 1H), 7.38-7.41(m, 2H), 7.73(s, 1H), 7.86-7.88(m, 1H), 8-8.03(m, 1H)	ESI+ 526(100)
264	 C23H27Cl2N5O2S2	>90 結晶 >220	DMSO-d6-400 0.89-0.9(m, 4H), 1.93(br, 1H), 2.96(s, 3H), 2.98(s, 3H), 3.56(br, 2H), 4.35(s, 2H), 4.74(br, 2H), 7.32(s, 1H), 7.36-7.38(m, 2H), 7.42-7.51(m, 2H), 10.29(br, 1H), 12.37(s, 1H)	ESI+ 504(100), 506(40)

[0154]

[Table 68]

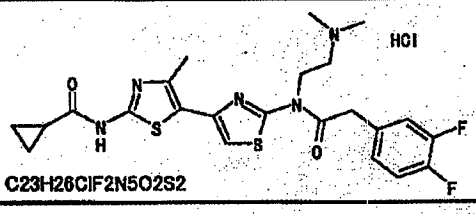
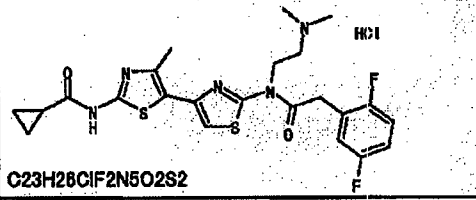
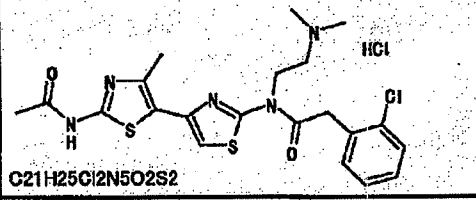
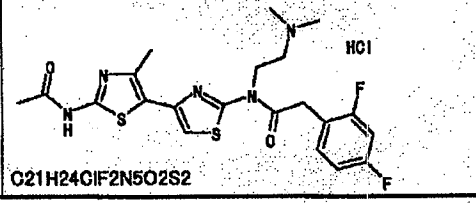
表 67

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
265	 C23H26Cl3N5O2S2	>90 結晶 >220	DMSO-d6-400 0.89-0.9(m, 4H), 1.93(br, 1H), 2.62(br, 2H), 3.26(s, 6H), 4.35(s, 2H), 4.55(br, 2H), 7.28(s, 1H), 7.47(s, 2H), 7.68(s, 1H), 10.11(br, 1H), 12.31(s, 1H)	ESI+ 538(100), 540(70)
266	 C25H32ClN5O4S2	>90 アモルファス	DMSO-d6-400 0.89-0.9(m, 4H), 1.93(br, 1H), 3.29(s, 6H), 3.75(s, 6H), 4.09(s, 2H), 4.34(br, 2H), 6.77-6.80(m, 1H), 6.91-6.94(m, 2H), 7.24(s, 1H), 12.31(s, 1H)	ESI+ 530(100)
267	 C24H30ClN5O3S2	>90 結晶 >220	DMSO-d6-300 0.89-0.9(m, 4H), 1.93(br, 1H), 2.95(s, 3H), 2.97(s, 3H), 3.52(s, 6H), 3.75(s, 3H), 4.09(s, 2H), 4.7(br, 2H), 6.93(dd, 1H, J=7.44, 7.4Hz), 7.02(d, 1H, J=8.08Hz), 7.2(d, 1H, J=7.46Hz), 7.23(s, 1H), 7.29(dd, 1H, J=8.01, 7.64Hz), 10.58(br, 1H), 12.31(s, 1H)	ESI+ 500(100)
268	 C23H26ClF2N5O2S2	>90 結晶 >220	DMSO-d6-400 0.89-0.9(m, 4H), 1.93(br, 1H), 2.96(s, 6H), 3.52(br, 2H), 4.33(s, 2H), 4.7(br, 2H), 7.16(dd, 1H, J=7.9, 7.8Hz), 7.33(s, 1H), 7.46-7.51(m, 1H), 12.37(s, 1H)	ESI+ 506(100)

[0155]

[Table 69]

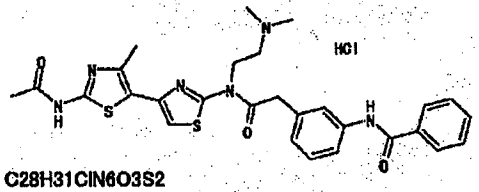
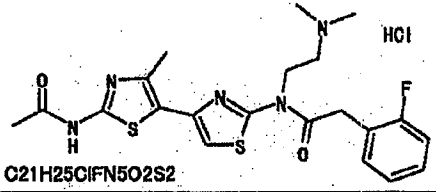
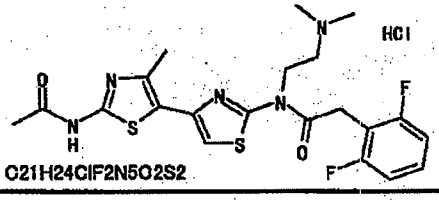
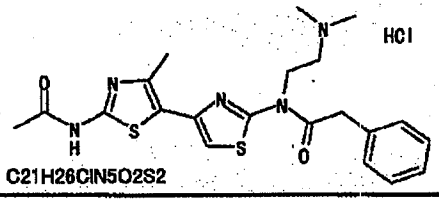
表 68

実施例番号	構造式 / 組成式	純度(%) / 性状 / 融点(℃)	1H NMR(δ)ppm	MS
269	 C23H26ClF2N5O2S2	>90 結晶 >220	DMSO-d6-400 0.89-0.9(m, 4H), 1.93(br, 1H), 2.94(s, 6H), 3.49(br, 2H), 4.25(s, 2H), 4.65(br, 2H), 7.14(br, 1H), 7.31(s, 1H), 7.42-7.48(m, 1H), 10.63(br, 1H), 12.37(s, 1H)	ESI+ 506(100)
270	 C23H26ClF2N5O2S2	>90 結晶 >220	DMSO-d6-400 0.89-0.9(m, 4H), 1.93(br, 1H), 2.96(s, 6H), 3.49(br, 2H), 4.3(s, 2H), 4.69(br, 2H), 7.21-7.32(m, 4H), 10.49(br, 1H), 12.37(s, 1H)	ESI+ 506(100)
271	 C21H25Cl2N5O2S2	>90 結晶 234 - 236	DMSO-d6-300 2.14(s, 3H), 2.49(s, 3H), 2.95(s, 3H), 2.97(s, 3H), 3.56(br, 2H), 4.37(s, 2H), 4.74-4.76(m, 2H), 7.33-7.38(m, 3H), 7.45-7.48(m, 2H)	ESI+ 478(100)
272	 C21H24ClF2N5O2S2	>90 結晶 157 - 159.5	DMSO-d6-300 2.14(s, 3H), 2.49(s, 3H), 2.94(s, 3H), 2.96(s, 3H), 3.56-3.58(m, 2H), 4.3(s, 2H), 4.7-4.72(m, 2H), 7.1-7.12(m, 1H), 7.26-7.28(m, 1H), 7.33(s, 1H), 7.46(s, 1H)	ESI+ 480(100)

[0156]

[Table 70]

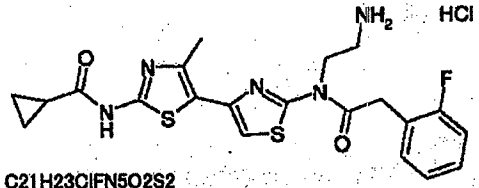
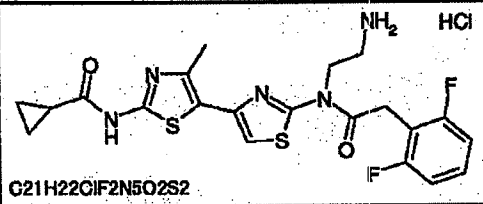
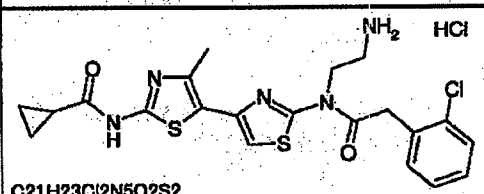
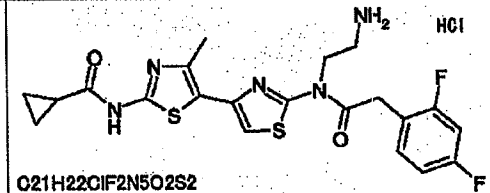
表 69

実施例番号	構造式 ／ 組成式	純度(%) ／性状／ 融点(℃)	1H NMR(δ)ppm	MS
273	 C28H31ClN6O3S2	>90 結晶 182 - 185	DMSO-d6-300 2.14(s, 3H), 2.5(s, 3H), 2.94(s, 3H), 2.95(s, 3H), 3.51-3.53(m, 2H), 4.23(s, 2H), 4.64-4.66(m, 2H), 7.12-7.14(m, 1H), 7.33-7.35(m, 2H), 7.52-7.59(m, 3H), 7.66-7.67(m, 1H), 7.82(s, 1H), 7.97(d, 2H, J=9Hz)	ESI+ 563(100)
274	 C21H25ClFN5O2S2	>90 アモルファス	DMSO-d6-300 2.14(s, 3H), 2.96(s, 3H), 2.98(s, 3H), 4.29(s, 2H), 4.58(br, 2H), 7.19-7.29(m, 2H), 7.34(s, 1H), 7.35-7.42(m, 2H), 10.49(br, 1H), 12.11(s, 1H)	ESI+ 462(100)
275	 C21H24ClF2N5O2S2	>90 アモルファス	DMSO-d6-300 2.14(s, 3H), 2.79(br, 6H), 4.34(s, 2H), 4.62(br, 2H), 7.16(d, 1H, J=8.02Hz), 7.18(d, 1H, J=7.79Hz), 7.33(s, 1H), 7.42-7.48(m, 1H), 10.46(br, 1H), 12.10(s, 1H)	ESI+ 480(100)
276	 C21H26ClN5O2S2	>90 アモルファス	DMSO-d6-300 2.14(s, 3H), 2.94(s, 6H), 3.49(br, 2H), 4.21(s, 2H), 4.62(br, 2H), 7.32-7.36(m, 6H), 10.46(br, 1H), 12.09(s, 1H)	ESI+ 444(100)

[0157]

[Table 71]

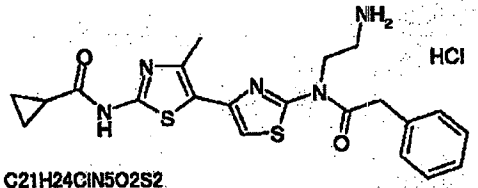
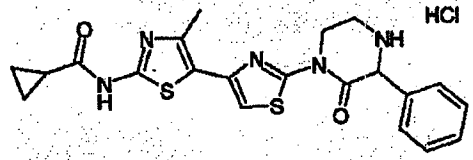
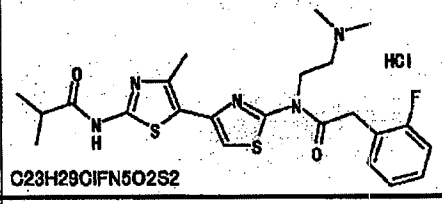
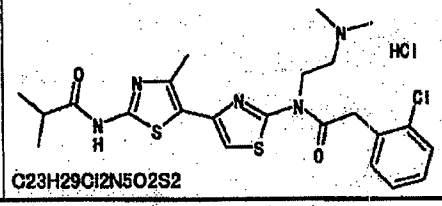
表 70

実施例番号	構造式 / 組成式	純度 (%) / 性状 / 融点 (°C)	1H NMR(δ)ppm	MS
277	 C21H23ClFN5O2S2	>90 アモルファス	DMSO-d6-300 0.84-0.98(m, 4H), 1.90-2.01(m, 1H), 2.48(s, 3H), 3.29-3.43(m, 2H), 4.27(s, 2H), 4.48-4.60(m, 2H), 7.18-7.45(m, 5H), 8.25(br, 3H), 12.41(s, 1H)	ESI+ 460(100)
278	 C21H22ClF2N5O2S2	>90 アモルファス	DMSO-d6-400 0.84-0.97(m, 4H), 1.91-1.99(m, 1H), 2.48(s, 3H), 3.27-3.38(m, 2H), 4.33(s, 2H), 4.54-4.63(m, 2H), 7.16(t, 2H, J=7.85Hz), 7.31(s, 1H), 7.4-7.5(m, 1H), 8.31(br, 3H), 12.39(br, 1H)	ESI+ 478(100)
279	 C21H23Cl2N5O2S2	>90 アモルファス	DMSO-d6-300 0.84-0.98(m, 4H), 1.89-2.01(m, 1H), 2.48(s, 3H), 3.29-3.45(m, 2H), 4.35(s, 2H), 4.49-4.63(m, 2H), 7.26-7.55(m, 5H), 8.31(br, 3H), 12.41(br, 1H)	ESI+ 476(100)
280	 C21H22ClF2N5O2S2	>90 アモルファス	DMSO-d6-300 0.83-0.98(m, 4H), 1.90-2.01(m, 1H), 2.48(s, 3H), 3.27-3.46(m, 2H), 4.27(s, 2H), 4.45-4.62(m, 2H), 7.12(t, 1H, J=8.4Hz), 7.28(t, 1H, J=9.8Hz), 7.32(s, 1H), 7.47(q, 1H, J=8.4Hz), 8.29(br, 3H), 12.41(br, 1H)	ESI+ 478(100)

[0158]

[Table 72]

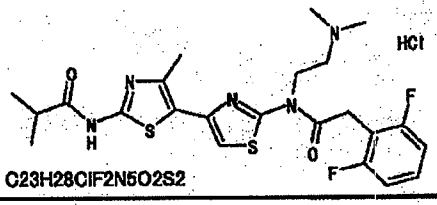
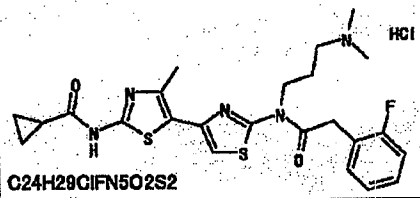
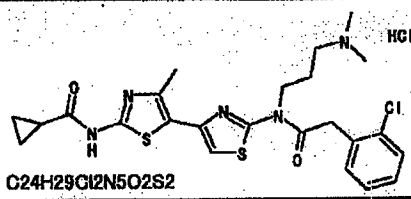
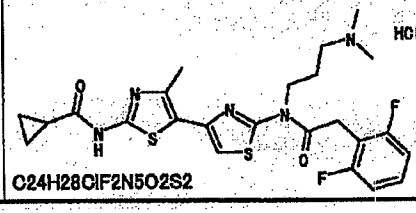
表 71

実施例番号	構造式 / 組成式	純度(%) / 性状 / 融点(℃)	1H NMR(δ)ppm	MS
281	 C21H24ClN5O2S2	>90 アモルファス	DMSO-d6-400 0.83-0.96(m, 4H), 1.91-2.00(m, 1H), 2.47(s, 3H), 3.28-3.41(m, 2H), 4.21(s, 2H), 4.42-4.51(m, 2H), 7.26-7.38(m, 6H), 8.32(br, 3H), 12.36(br, 1H)	ESI+ 442(100)
282	 C21H22ClN5O2S2	>90 アモルファス	DMSO-d6-300 0.84-0.97(m, 4H), 1.90-2.01(m, 1H), 2.51(s, 3H), 3.66-3.80(m, 2H), 4.54-4.63(m, 2H), 5.66(s, 1H), 7.43(s, 1H), 7.46-7.66(m, 5H), 10.48(br, 1H), 10.84(br, 1H), 12.44(br, 1H)	ESI+ 440(100)
283	 C23H29ClFN5O2S2	>90 結晶 155 - 161	DMSO-d6-300 1.1(s, 3H), 1.13(s, 3H), 2.49(s, 3H), 2.72-2.74(m, 1H), 2.96(s, 3H), 2.98(s, 3H), 3.56-3.58(m, 2H), 4.3(s, 2H), 4.5-4.6(m, 2H), 7.2-7.22(m, 2H), 7.33(s, 1H), 7.39-7.41(m, 2H)	ESI+ 490(100)
284	 C23H29Cl2N5O2S2	>90 結晶 >230	DMSO-d6-300 1.11(s, 3H), 1.13(s, 3H), 2.49(s, 3H), 2.72-2.74(m, 1H), 2.97(s, 3H), 2.99(s, 3H), 3.56-3.58(m, 2H), 4.36(s, 2H), 4.72-4.74(m, 2H), 7.33-7.38(m, 3H), 7.45-7.48(m, 2H)	ESI+ 506(100)

[0159]

[Table 73]

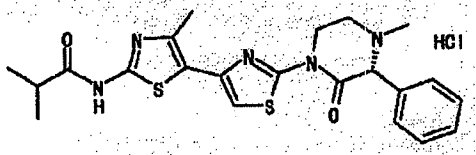
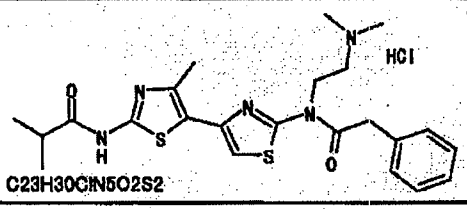
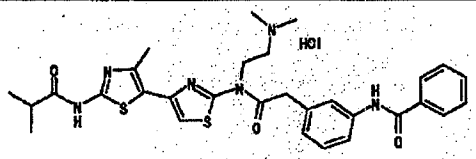
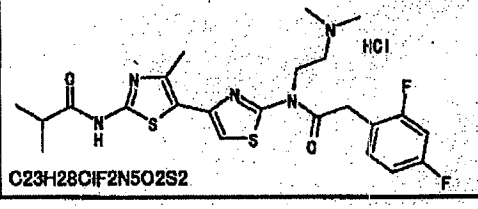
表 72

実施例番号	構造式 / 組成式	純度(%) / 性状 / 融点(℃)	1H NMR(δ)ppm	MS
285	 C23H28ClF2N5O2S2	>90 結晶 >230	DMSO-d6-300 1.11(s, 3H), 1.13(s, 3H), 2.49(s, 3H), 2.72-2.74(m, 1H), 2.96(s, 3H), 2.98(s, 3H), 3.56-3.58(m, 2H), 4.35(s, 2H), 4.74-4.76(m, 2H), 7.17(t, 2H, J=7.5Hz), 7.34(s, 1H), 7.45-7.47(m, 1H)	ESI+ 508(100)
286	 C24H29ClFN5O2S2	>90 結晶 226 - 228	DMSO-d6-300 0.89-0.93(m, 4H), 1.94-1.98(m, 1H), 2.25-2.28(m, 2H), 2.49(s, 3H), 2.78(s, 3H), 2.8(s, 3H), 3.23-3.25(m, 2H), 4.24(s, 2H), 4.35-4.37(m, 2H), 7.18-7.29(m, 2H), 7.29(s, 1H), 7.34-7.43(m, 2H)	ESI+ 502(100)
287	 C24H29Cl2N5O2S2	>90 結晶 217 - 219	DMSO-d6-300 0.89-0.93(m, 4H), 1.94-1.98(m, 1H), 2.25-2.28(m, 2H), 2.49(s, 3H), 2.79(s, 3H), 2.8(s, 3H), 3.23-3.25(m, 2H), 4.31(s, 2H), 4.37-4.39(m, 2H), 7.28(s, 1H), 7.34-7.37(m, 2H), 7.44-7.51(m, 2H)	ESI+ 518(100)
288	 C24H28ClF2N5O2S2	>90 結晶 >230	DMSO-d6-300 0.89-0.93(m, 4H), 1.94-1.98(m, 1H), 2.25-2.28(m, 2H), 2.49(s, 3H), 2.79(s, 3H), 2.8(s, 3H), 3.25-3.26(m, 2H), 4.27(s, 2H), 4.39-4.41(m, 2H), 7.13-7.18(m, 2H), 7.3(s, 1H), 7.42(s, 2H)	ESI+ 520(100)

[0160]

[Table 74]

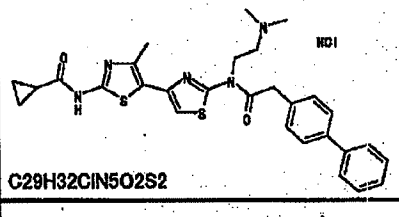
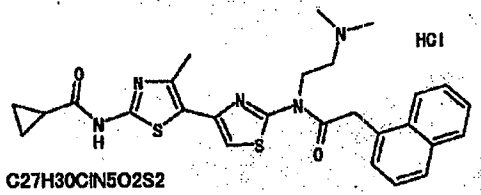
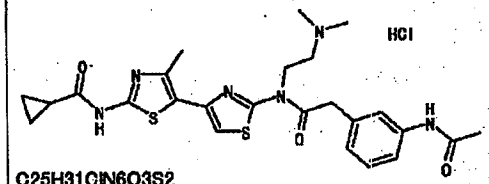
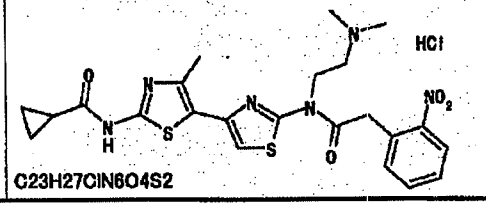
表 73

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
289	 C22H26ClN5O2S2	>90 結晶 227.7 - 232.4	DMSO-d6-400 1.13(d, 6H, J=6.85Hz), 2.55(br, 1H), 2.7-2.78(m, 1H), 3.8(br, 5H), 4.68(br, 1H), 4.62(br, 1H), 7.39(s, 1H), 7.47(br, 3H), 7.6(br, 2H), 12.09(s, 1H)	ESI+ 456(100)
290	 C23H30ClN5O2S2	>90 結晶 >220	DMSO-d6-300 1.12(d, 6H, J=6.57Hz), 2.7-2.76(m, 1H), 2.95(s, 3H), 2.96(s, 3H), 3.51(br, 5H), 4.22(s, 2H), 4.65(br, 1H), 7.32-7.36(m, 6H), 10.52(br, 1H), 12.05(s, 1H)	ESI+ 472(100)
291	 C30H35ClN6O3S2	>90 アモルファス	DMSO-d6-300 1.12(d, 6H, J=6.96Hz), 2.7-2.76(m, 1H), 2.95(s, 3H), 2.96(s, 3H), 3.51(br, 2H), 4.24(s, 2H), 4.65(br, 2H), 7.09(d, 1H, J=7.68Hz), 7.32-7.36(m, 2H), 7.52-7.6(m, 3H), 7.68(d, 1H, J=7.92Hz), 7.82(s, 1H), 7.96-7.98(m, 2H), 10.3(s, 1H), 10.52(br, 1H), 12.12(s,	ESI+ 591(100)
292	 C23H28ClF2N5O2S2	>90 結晶 >220	DMSO-d6-400 1.12(d, 6H, J=6.86Hz), 2.68-2.75(m, 1H), 2.97(s, 6H), 3.58(br, 2H), 4.28(s, 2H), 4.7(br, 2H), 7.09-7.14(m, 1H), 7.24-7.3(m, 1H), 7.35(s, 1H), 7.41-7.49(m, 1H), 10.41(br, 1H), 12(s, 1H)	ESI+ 508(100)

[0161]

[Table 75]

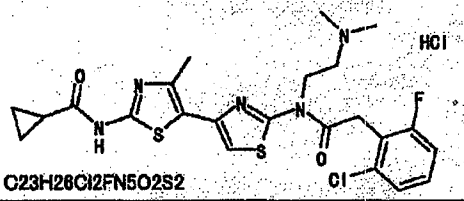
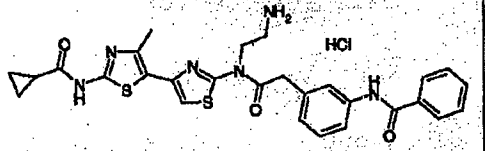
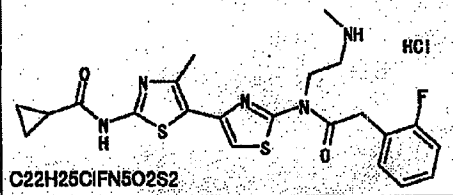
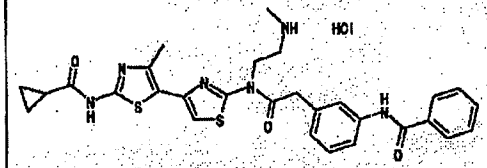
表 74

実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
293	 C29H32ClN5O2S2	>90 結晶 121 - 123	DMSO-d6-300 0.89-0.93(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 2.92(s, 3H), 2.93(s, 3H), 3.5-3.6(m, 2H), 4.28(s, 2H), 4.65-4.7(m, 2H), 7.31-7.5(m, 6H), 7.64-7.69(m, 4H)	ESI+ 546(100)
294	 C27H30ClN5O2S2	>90 結晶 >220	DMSO-d6-300 0.89-0.93(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 2.96(s, 3H), 2.98(s, 3H), 3.62-3.67(m, 2H), 4.71(s, 2H), 4.75-4.85(m, 2H), 7.29(s, 1H), 7.49-7.55(m, 4H), 7.88-7.98(m, 3H)	ESI+ 520(100)
295	 C25H31ClN6O3S2	>90 結晶 162 - 167	DMSO-d6-300 0.89-0.93(m, 4H), 1.94-1.98(m, 1H), 2(s, 3H), 2.49(s, 3H), 2.91(s, 3H), 2.92(s, 3H), 3.45-3.5(m, 2H), 4.19(s, 2H), 4.6-4.65(m, 2H), 7.04(d, 1H, J=9Hz), 7.24-7.31(m, 2H), 7.48(d, 1H, J=6Hz), 7.57(s, 1H)	ESI+ 527(100)
296	 C23H27ClN6O4S2	>90 結晶 >220	DMSO-d6-300 0.89-0.93(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 2.96(s, 3H), 2.98(s, 3H), 3.5-3.6(m, 2H), 4.68(s, 2H), 4.75-4.85(m, 2H), 7.31(s, 1H), 3.65(m, 2H), 7.79-7.81(m, 1H), 8.17-8.2(m, 1H)	ESI+ 515(100)

[0162]

[Table 76]

表 75

実施例番号	構造式 / 組成式	純度(%) / 性状 / 融点(℃)	1H NMR(δ)ppm	MS
297	 C23H26Cl2FN5O2S2	>90 結晶 >220	DMSO-d6-300 0.89-0.93(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 2.95(s, 3H), 2.96(s, 3H), 3.5-3.6(m, 2H), 4.43(s, 2H), 4.75-4.78(m, 2H), 7.25-7.5(m, 4H)	ESI+ 522(100)
298	 C28H29ClN6O3S2	>90 アモルファス	DMSO-d6-300 0.84-0.94(m, 4H), 1.87-1.96(m, 1H), 2.43(s, 3H), 3.26-3.38(m, 4H), 3.43(s, 2H), 6.65(s, 1H), 7.01(d, 1H, J=7.7Hz), 7.27(t, 1H, J=7.7Hz), 7.51-7.60(m, 3H), 7.66(d, 1H, J=7.7Hz), 7.7(s, 1H), 7.97(d, 2H, J=8.1Hz), 8.24(br, 2H), 10.24(s, 2H), 12.30(s, 2H)	ESI+ 561(100)
299	 C22H25ClFN5O2S2	>90 結晶 121 - 123	DMSO-d6-300 0.89-0.93(m, 4H), 1.94-1.98(m, 1H), 2.49(s, 3H), 2.65(s, 3H), 3.4-3.45(m, 2H), 4.31(s, 2H), 4.6-4.65(m, 2H), 7.18-7.24(m, 2H), 7.3(s, 1H), 7.36-7.42(m, 2H)	ESI+ 474(100)
300	 C29H31ClN6O3S2	>90 結晶 118 - 121	DMSO-d6-300 0.89-0.93(m, 4H), 1.91-1.97(m, 1H), 2.49(s, 3H), 2.65(s, 3H), 3.4-3.43(m, 2H), 4.2(s, 2H), 4.5-4.6(m, 2H), 7.12(d, 1H, J=9Hz), 7.3-7.36(m, 2H), 7.5-7.59(m, 3H), 7.66(d, 1H, J=6Hz), 7.81(s, 1H), 7.96(d, 2H, J=6Hz)	ESI+ 575(100)

[0163]
[Table 77]

表 76

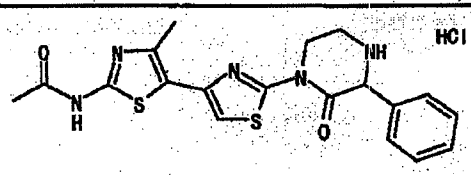
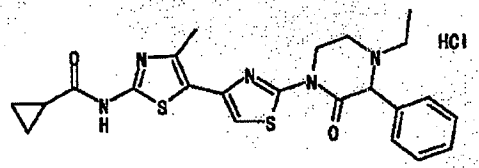
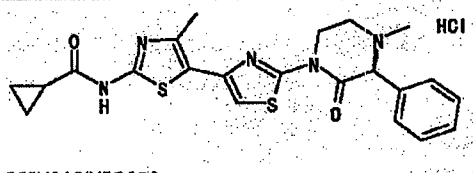
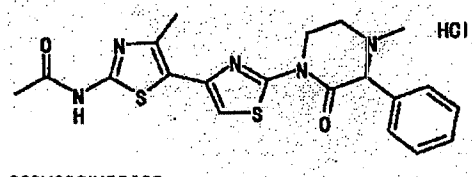
実施例番号	構造式 ／ 組成式	純度 (%) ／性状／ 融点 (℃)	1H NMR(δ)ppm	MS
301	 C19H20ClN5O2S2	>90 結晶 >220	DMSO-d6-300 2.15(s, 3H), 3.75(br, 2H), 4.57(br, 2H), 5.65(s, 2H), 7.43(s, 1H), 7.5(br, 3H), 7.58(br, 2H), 12.11(s, 1H)	ESI+ 414(100)
302	 C23H26ClN5O2S2	>90 アモルファス	DMSO-d6-300 0.89-0.9(m, 4H), 1.18(br, 3H), 1.93(br, 1H), 4.44(br, 7H), 7.38(s, 1H), 7.45(br, 3H), 7.6(br, 2H), 12.39(s, 1H)	ESI+ 468(100)
303	 C22H24ClN5O2S2	>90 結晶 >220	DMSO-d6-400 0.89-0.9(m, 4H), 1.93(br, 1H), 2.61(br, 2H), 4.01(br, 3H), 4.44(br, 1H), 4.6(br, 1H), 5.26(br, 1H), 7.39(s, 1H), 7.47(br, 3H), 7.8(br, 2H), 12.34(s, 1H)	ESI+ 454(100)
304	 C20H22ClN5O2S2	>90 結晶 >220	DMSO-d6-300 2.15(s, 3H), 2.63(br, 2H), 4.07(br, 3H), 4.6(br, 2H), 5.43(br, 1H), 7.42(s, 1H), 7.49(br, 3H), 7.62(br, 2H), 12.09(s, 1H)	ESI+ 428(100)

表 77

実施例番号	構造式／組成式	純度(%)／性状／融点(℃)	1H NMR(δ)ppm	MS
305	C19H24Cl2FN5OS2	>80 結晶 >220	DMSO-d6-300 2.43(s, 3H), 2.93(s, 3H), 2.95(s, 3H), 3.54(br, 2H), 4.31(s, 2H), 4.7(br, 2H), 7.19-7.25(m, 2H), 7.27-7.43(m, 2H)	ESI+ 420(100)
306	C26H30Cl2N6O2S2	>90 アモルファス	DMSO-d6-400 2.42(s, 3H), 2.92(s, 3H), 2.93(s, 3H), 3.48(br, 2H), 4.24(s, 2H), 4.65(br, 2H), 7.13(d, 1H, J=7.48Hz), 7.35(dd, 1H, J=7.88, 7.8Hz), 7.42(s, 1H), 7.51-7.61(m, 3H), 7.67(d, 1H, J=8.44Hz), 7.83(s, 1H), 7.96-7.98(m, 2H), 9.11(br, 1H), 10.29(s, 1H), 10.92(br,	ESI+ 521(100)

[0164]Next, the measuring method of the PKC inhibiting activity of this invention compound is explained.

Example of an examination [1] After mixing PKC enzyme activity examination substrate mixed liquor and a specimen material solution at a rate of 10:1, the enzyme solution was added in

equivalent amount with substrate mixed liquor, and it incubated at 37 ** for 15 minutes. After adding 300mM orthophosphoric acid in equivalent amount with substrate mixed liquor as a reaction stop agent and stopping a reaction, Reaction mixture was spotted on the phosphocellulose paper (the product made by Whatman, and P-81), and after 75mM orthophosphoric acid washed twice, radioactivity was measured with the bio-imaging analyzer (BAS2500, product made by Fuji film). The rate of the radioactivity at the time of adding a specimen material over the radioactivity at the time of adding DMSO was searched for, and from the inhibition rate of each concentration, IC_{50} value was computed and it was considered as the index of inhibiting activity. A result is shown in Table 89 from Table 78.

Specimen-material solution: Subject goods were dissolved in dimethyl sulfoxide (DMSO), and it diluted so that it might be set to final concentration 10nM-10microM.

Substrate mixed liquor : 200microM calcium chloride, 10 mM magnesium chloride, 2microM ATP, 60micro g/mlL-alpha-phosphatidyl-L-serine, 6 microg/ml 1, 2-dioleoyl-sn-glycerol (C18:1, [cis]-9), It is made to dissolve in 50 mM Tris/HCl (pH 7.5) so that it may become Triton X-100 or 5microM myelin BASIC protein 0.02%, [gamma-32P] ATP (the product made by Amersham and cat. No. PB168) was added so that it might become in ml and 60 microcurie /.

Enzyme solution :P KC enzyme preparation (Protein Kinase C, Human Recombinant, product made by CALBIOCHEM), It diluted so that it might become the amount of enzymes in which about 5% of ATP is used by the reaction in this enzyme activity examination in [examined substance] not adding using an assay buffer (10mM Hepes pH 7.4, 0.01% Triton X-100).

[0165]Example of an examination [2] Formalin Since a test exam is comparatively similar to the symptoms after a peripheral human organization injury, it is an in vivo examination mostly used in examination of an analgesic effect. The rat (Crj, SD, 7 or 8 weeks old, male) was abstained from food in the fast cage on the day preceding test implementation. It was suspended in MC solution 0.5%, and the specimen material was administered orally to the rat. After carrying out subcutaneous injection of the solution which diluted the saturation formalin solution with the physiological saline 20 times to the left hind-foot vola part of a rat 2 hours after administration, the number of seconds of the action in which a rat licks a left hind foot even in 15 to 30 minutes (the II phase) was measured even the 5-minute back (the Ith phase) of an immediately after [administration]. The backward one and the significant difference over the solvent administration group of the number of seconds to the 15 to 30-minute backward were examined for after [formalin subcutaneous injection] 5 minutes using Dunnet test, respectively. A result is shown in Table 90.

[0166]

[Table 78]

表７８

実施例番号	PKC活性阻害 $IC_{50}(\mu M)$		
	PKCα	PKCβII	PKCγ
1	0.8691	2.9062	0.0369
2	0.6811	2.0681	0.0505
3	0.640	2.70	0.049
4	0.9238	2.0825	0.0966
5	1.00	2.60	0.096
6	1.0342	1.6049	0.3559
7	0.381	3.1067	0.2181
9	3.1034	5.8587	0.6783
10	100	100	0.9605
12	2.2365	3.2109	0.7864
14	0.484	0.8281	0.3475
15	0.6744	1.5877	0.4428
16	1.5652	2.8276	0.3887
17	1.9997	1.9916	0.3033
20	0.4222	2.5555	0.1314
22	0.2146	1.1874	0.2336
23	0.2607	1.5836	0.1846
24	0.7288	0.7508	0.1422
25	1.1193	1.0252	0.2364
26	0.4024	0.6619	0.1003
27	0.7984	2.1487	0.3068

[0167]
[Table 79]

表７９

実施例番号	PKC活性阻害 $IC_{50}(\mu M)$		
	PKCα	PKCβII	PKCγ
28	20.9551	58.7021	0.7796
30	1.1229	2.3889	0.1452
31	0.8852	2.2086	0.3141
32	0.8931	10	0.2666
33	0.5861	0.8481	0.2966
34	1.3769	3.403	0.5586
36	0.1011	0.2243	0.1
38	1.0239	2.3066.	0.2804
39	1.6275	2.3583	0.4253
40	3.7545	9.3437	0.4791
41	0.7993	1.6952	0.3414
43	1.8608	2.9152	0.3758
44	4.2445	18.6092	0.505
50	0.1253	0.4761	0.1
56	1.9705	3.2759	0.6389
57	0.3019	0.7948	0.047
58	0.2356	0.7665	0.0431
59	0.0861	0.3512	0.0234
60	0.0982	0.3345	0.0274
61	0.3514	1.328	0.1123
62	0.0713	0.1727	0.0286

[0168]

[Table 80]

表８０

実施例番号	PKC活性阻害 $IC_{50}(\mu M)$		
	PKCα	PKCβII	PKCγ
63	0.1384	0.4357	0.0389
64	0.1084	0.2647	0.0383
65	0.2031	0.5139	0.0546
66	0.0829	0.2596	0.0305
67	0.1377	0.503	0.0643
68	0.7166	2.5578	0.1621
69	0.5753	3.0038	0.1886
70	0.369	1.8323	0.0914
77	0.1811	1.1455	0.0436
78	0.3671	4.4274	0.0377
79	6.1068	10	0.4187
85	0.4281	0.0817	0.0518
86	10	10	0.4095
87	4.2331	10	0.6303
89	0.4605	0.8827	0.1468
91	0.3335	0.9374	0.0645
95	0.1558	0.4456	0.0289
96	0.6069	0.978	0.2311
97	0.6261	1.3975	0.6133
101	0.4178	5.2222	0.1573
102	0.0814	0.3242	0.0438

[0169]

[Table 81]

表８１

実施例番号	PKC活性阻害 $IC_{50}(\mu M)$		
	PKCα	PKCβII	PKCγ
104	0.2578	0.4058	0.0555
105	0.2559	0.3638	0.0569
106	0.1656	0.3231	0.301
107	0.1257	0.2503	0.0292
108	0.2942	0.4942	0.0815
109	0.01	0.0253	0.01
110	1.0028	2.5185	0.3547
111	0.2484	0.6543	0.0885
112	0.0582	0.1389	0.0266
113	0.1352	0.4307	0.2066
117	0.1486	0.2804	0.0411
118	0.1303	0.3481	0.0252
119	0.5804	0.7109	0.1313
120	0.5003	1.121	0.1835
121	0.043	0.0849	0.0315
122	10	10	0.2648
123	0.231	0.3928	0.0667
124	0.605	4.005	0.176
125	0.1213	0.7247	0.0374
126	0.4539	0.8748	0.0696
127	0.1409	0.5416	0.0358

[0170]
[Table 82]

表８２

実施例番号	PKC活性阻害 $IC_{50}(\mu M)$		
	PKCα	PKCβII	PKCγ
128	0.6411	1.3177	0.0832
129	0.7891	10	0.1053
130	0.4813	2.6958	0.0778
131	0.3694	1.0981	0.0458
132	10	10	0.3842
133	0.7601	7.2341	0.2096
134	0.6145	10	0.1126
135	10	10	0.4226
136	0.3835	0.5662	0.0477
137	0.6491	0.6733	0.114
138	0.206	0.7927	0.0731
139	0.039	0.18	0.0233
140	0.6994	4.4524	0.2783
141	4.3222	10	0.6945
142	0.5658	3.4076	0.262
143	2.4709	2.8369	0.238
144	1.8262	5.1504	0.2386
145	10	10	0.4329
147	10	10	0.3341
148	0.7315	2.2953	0.1236
149	0.2026	0.4703	0.022

[0171]

[Table 83]

表８３

実施例番号	PKC活性阻害 $IC_{50}(\mu M)$		
	PKCα	PKCβII	PKCγ
150	0.2403	0.6434	0.034
151	4.1609	10	0.586
152	1.3969	0.2374	0.1091
153	10	10	0.7554
156	0.0817	0.6858	0.037
157	0.2053	10	0.0854
158	0.8114	2.2487	0.1631
159	0.4899	1.4472	0.0722
160	0.5408	0.1689	0.048
161	0.7628	0.2478	0.0549
162	10	0.3797	0.2692
163	10	9.3292	0.3971
164	0.6204	3.0762	0.2238
165	0.4699	10	0.0439
166	1.8756	10	0.8109
167	0.7312	10	0.2404
168	10	10	0.2727
169	0.6706	10	0.0535
170	0.01	0.0528	0.0115
171	0.01	0.0278	0.01
172	0.2315	2.284	0.0693

[0172]

[Table 84]

表８４

実施例番号	PKC活性阻害 $IC_{50}(\mu M)$		
	PKCα	PKCβII	PKCγ
173	0.1803	0.823	0.0227
178	0.2014	1.0955	0.0589
179	0.2014	1.0955	0.0589
180	0.0447	0.1852	0.0148
182	0.493	10	0.0632
183	0.5188	10	0.0655
185	4.5305	9.0984	0.7888
187	0.7463	2.4368	0.0677
188	3.1367	3.8826	0.3118
189	0.5497	1.2724	0.0648
190	0.2765	0.9269	0.0327
191	0.3441	1.4509	0.05
192	0.1874	0.6329	0.0411
193	0.3171	1.0387	0.0435
194	3.1816	10	0.7699
195	4.1963	6.8348	0.6202
196	3.118	4.2776	0.3954
197	0.5301	1.3578	0.0947
198	2.2416	0.7359	0.2847
199	3.5292	1.735	0.5815
200	2.7132	0.504	0.3708

[0173]

[Table 85]

表８５

実施例番号	PKC活性阻害 $IC_{50}(\mu M)$		
	PKCα	PKCβII	PKCγ
201	0.4534	0.0583	0.0326
202	0.1438	0.2821	0.0126
203	0.0181	0.0509	0.01
204	0.2536	0.6034	0.0752
205	1.8445	2.0435	0.6881
206	0.3621	0.7343	0.0497
207	1.2896	2.9182	0.0576
208	0.5169	1.4617	0.0229
209	5.1562	8.5936	0.4971
210	0.2416	0.7747	0.07
211	0.324	0.0546	0.0345
213	1.0162	4.1203	0.0976
214	0.0899	0.3258	0.0287
215	1.2266	2.6531	0.3828
216	1.5912	1.7024	0.3088
217	0.3023	0.8786	0.0569
218	0.6108	1.9878	0.0415
219	0.3836	1.0157	0.0425
220	1.7341	3.5649	0.082
221	1.1928	3.2046	0.1244
222	1.4298	4.8165	0.4648

[0174]

[Table 86]

表８６

実施例番号	PKC活性阻害 $IC_{50}(\mu M)$		
	PKCα	PKCβII	PKCγ
223	1.1599	3.0946	0.2411
224	0.6074	1.3187	0.1009
225	0.8434	2.0511	0.1088
226	1.2533	2.0744	0.0987
227	4.6416	10	0.3154
228	0.1439	0.527	0.0377
230	0.7932	10	0.1519
231	1.9148	4.3648	0.6877
232	2.2058	4.3243	0.7279
233	1.1948	7.5429	0.2491
234	3.3771	10	0.642
237	0.0664	0.2718	0.0753
238	0.1643	0.4521	0.1138
239	0.1645	0.3851	0.1128
240	2.0602	4.4752	0.1667
241	1.6723	3.275	0.2455
242	1.5715	3.9299	0.1314
243	0.5143	2.0035	0.0327
244	1.6825	4.5809	0.1265
245	4.5598	7.7718	0.3007
246	4.1918	7.8553	0.269

[0175]

[Table 87]

表8.7

実施例番号	PKC活性阻害 $IC_{50}(\mu M)$		
	PKCα	PKCβII	PKCγ
247	0.7353	1.4122	0.1574
248	4.7388	3.0942	0.2127
250	2.2456	3.8395	0.3516
251	1.2051	3.3082	0.1165
252	7.5785	9.9982	0.1643
253	0.7711	1.6616	0.0908
255	8.7832	10	0.3636
256	0.6817	2.1602	0.1743
257	0.0197	0.0574	0.013
258	0.5716	1.8643	0.0434
259	2.3994	10	0.129
260	0.5492	1.9493	0.038
261	3.3157	8.2864	0.3605
262	2.7343	5.6371	0.7032
263	2.5549	0.9648	0.2083
264	0.3683	1.4796	0.0324
265	0.6817	2.5745	0.0588
267	1.4729	2.9851	0.2119
268	2.9237	5.219	0.073
269	2.3036	4.6499	0.2522
270	1.8292	3.7545	0.149

[0176]

[Table 88]

表８８

実施例番号	PKC活性阻害 $IC_{50}(\mu M)$		
	PKCα	PKCβII	PKCγ
271	0.8243	2.139	0.0606
272	1.2554	2.4596	0.0672
273	0.6934	1.4572	0.0297
274	1.7267	2.5746	0.0768
275	4.6116	5.5656	0.2395
276	2.7981	5.0732	0.2772
277	1.5974	2.902	0.121
278	4.7862	7.3154	0.3694
279	0.5391	2.1049	0.158
280	0.5228	1.8414	0.1874
281	2.028	4.1114	0.4423
282	0.9474	6.0803	0.1372
283	1.6883	2.3741	0.1019
284	3.2021	2.0008	0.2032
285	10	6.255	0.4102
286	0.2957	0.6491	0.0526
287	0.1501	0.3063	0.0503
288	1.6162	2.2667	0.3434
289	1.8581	2.2649	0.1214
290	9.5046	4.951	0.3994
291	1.978	1.79	0.0708

[0177]

[Table 89]

表８９

実施例番号	PKC活性阻害 $IC_{50}(\mu M)$		
	PKCα	PKCβII	PKCγ
292	2.7292	2.1358	0.1568
294	1.5731	2.9446	0.1406
295	1.70	5.90	0.076
296	2.0174	4.0763	0.2116
297	3.7313	5.8978	0.1485
299	2.0506	5.6728	0.2506
300	6.54	10	0.8001
301	4.0711	10	0.7776
302	2.2321	10	0.2145
305	3.8583	10	0.5705
306	1.3647	6.3833	0.2066

[0178]
[Table 90]

表９０

被験物質	投与量 (mg／kg)	リッキングタイム（秒）	
		第Ｉ相	第Ⅱ相
コントロール	－	151.9 ± 2.6	328.1 ± 7.4
1	3	148.5 ± 2.7	225.3 ± 7.6
	10	143.8 ± 3.8	199.9 ± 17.0
モルヒネ	10	129.0 ± 4.8	215.9 ± 13.0
コントロール	－	149.4 ± 2.7	317.5 ± 12.2
3	3	148.4 ± 4.3	209.5 ± 12.3
	10	146.4 ± 4.1	187.5 ± 11.1
モルヒネ	10	122.0 ± 3.3	216.5 ± 6.9
コントロール	－	153.6 ± 3.2	329.5 ± 5.5
5	3	145.6 ± 4.0	232.9 ± 9.7
	10	143.3 ± 5.2	203.8 ± 13.9
モルヒネ	10	117.9 ± 6.7	237.0 ± 7.3
コントロール	－	151.3 ± 3.9	277.9 ± 13.3
202	30	136.1 ± 8.4	163.9 ± 14.9
	100	132.4 ±4.1	145.8 ± 22.2
コントロール	－	150.4 ± 2.9	322.9 ± 8.6
208	3	148.8 ± 5.7	275.4 ± 12.1
コントロール	－	141.3 ± 3.6	300.9 ± 9.0
243	3	140.9 ± 4.5	250.6 ± 15.8
コントロール	－	146.0 ± 3.8	288.0 ± 8.8
268	10	128.1 ± 8.1	195.6 ± 28.9
	30	119.3 ± 7.0	185.8 ± 17.4
コントロール	－	147.3 ± 4.0	310.1 ± 5.8
274	3	141.8 ± 5.3	222.8 ± 14.0
コントロール	－	149.4 ± 2.7	317.5 ± 12.2
295	3	147.1 ± 4.6	218.1 ± 16.8

コントロール：溶媒のみ。
リッキングタイム：ラットが左後肢を舐める行動の時間。
被験物質の番号は、該当する実施例番号で合成された化合物を示す。

[0179]Although the example of pharmaceutical preparation is given to below, it is not limited to this.

Compound of the example (a) example 1 of pharmaceutical preparation 10g (b) milk sugar 50g (c) corn starch 15g (d) carboxymethylcellulose sodium 44g (e) magnesium stearate 1g (a), 30 g of the whole quantity of (b) and (c) and (d) is kneaded with water, and **** is performed after vacuum drying. 1000 tablets containing 10 mg per dose (a) are manufactured by mixing 14 g (d) and 1 g (e) in the end of this ****, and considering it as a tablet with a tableting machine.

[0180]

[Effect of the Invention]The thiazole compound of this invention shows high inhibiting activity to PKC, and the part is compared with PKCalpha, PKCbeta, and PKA, and shows the inhibitory

action to PKCgamma selectively so that clearly from the above-mentioned result. Therefore, these compounds serve as drugs which treat or/and prevent the condition relevant to PKC including mourning over tolerance over narcotic analgesics, such as a pain, a hyperalgesia, allodynia, and morphine, etc. The alternative operation to PKCgamma can serve as safe drugs in which remarkable side effects are not shown.

[Translation done.]

Applicants: Jingrong Cao et al.
Application No.: 10/696,862
Technology Center: 1600

RELATED PROCEEDINGS EVIDENCE

None